Interventions for dental fluorosis: A systematic review

Di Giovanni, Tamara ; Eliades, Theodore ; Papageorgiou, Spyridon N

Abstract: OBJECTIVE Dental fluorosis has considerable implications on the patients' quality of life. The present study assesses the comparative effectiveness of the various interventions for the treatment of fluorosed enamel. MATERIALS AND METHODS Nine databases were searched from inception to December 2016 for randomized trials. After duplicate study selection, data extraction, and risk of bias assessment, mean differences (MD) or Relative Risks and the corresponding 95% confidence intervals (CIs) were calculated and assessed with the GRADE approach. RESULTS Six trials with a total of 348 patients (at least 40% male/60% female) with a mean age of 17.7 years treated with bleaching, microabrasion, or resin infiltration were included. Evidence of low quality indicated that microabrasion resulted in smaller esthetic improvement compared to bleaching (MD = -2.9; 95% CI = -3.4 to -2.5). Evidence of moderate quality indicated that compared to bleaching a greater esthetic improvement was seen with resin infiltration (MD = 3.6; 95% CI = 2.7-4.6) or a combination of bleaching with resin infiltration (MD = 3.5; 2.8-3.7). However, all comparisons were supported from single trials and therefore caution is warranted. CONCLUSIONS Based on the existing limited evidence, resin infiltration seems to be the most promising treatment for dental fluorosis, followed by bleaching and microabrasion. CLINICAL SIGNIFICANCE For this systematic review, which was registered beforehand in PROSPERO (CRD42016053492), we synthesized evidence from existing randomized clinical trals on humans to see which treatment is most effective for the esthetic rehabilitation of dental fluorosis, the prevalence of which is seeing a worldwide steady increase. We found that resin infiltration seems to be the most effective treatment approach for lesions of mild to moderate severity, followed by bleaching, and finally microabrasion. Our study's strengths are its a priori registration, wide search, quality check according to Cochrane guidelines, and the use of a new robust analytic method to provide valid clinical recommendations according to the principles of evidence-based medicine.

DOI: https://doi.org/10.1111/jerd.12408

Interventions for dental fluorosis: a systematic review

Tamara DiGiovanni[1], Theodore Eliades, Dipl.DS, MS, Dr Med Sci, PhD, FIMMM, FRSC, FInstP[1], Spyridon N. Papageorgiou, DDS, Dr Med Dent[1]

[1]Clinic of Orthodontics and Pediatric Dentistry, Center of Dental Medicine, University of Zurich, Zurich, Switzerland

Running title: interventions for dental fluorosis

Keywords Dental fluorosis • Adverse effects • Esthetic rehabilitation • Treatment • Randomized clinical trials • Systematic review

Correspondence: Spyridon N. Papageorgiou, Clinic of Orthodontics and Pediatric Dentistry, Center of Dental Medicine, University of Zurich, Plattenstrasse 11, Zurich 8032, Switzerland; Tel: +41 44 634 32 87 / Fax: +41 44 634 43 35; e-mail: snpapage@gmail.com

Conflict of Interest

The authors of this manuscript certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

Abstract

Objective: Dental fluorosis has considerable implications on the patients' quality of life. The present study assesses the comparative effectiveness of the various interventions for the treatment of fluorosed enamel.

Materials and Methods: Nine databases were searched from inception to December 2016 for randomized trials. After duplicate study selection, data extraction, and risk of bias assessment, Mean Differences (MD) or Relative Risks (RR) and the corresponding 95% confidence intervals (CIs) were calculated and assessed with the GRADE approach.

Results: Six trials with a total of 348 patients (at least 40% male/ 60% female) with a mean age of 17.7 years treated with bleaching, microabrasion, or resin infiltration were included. Evidence of low quality indicated that microabrasion resulted in smaller esthetic improvement compared to bleaching (MD=-2.9; 95% CI=-3.4 to -2.5). Evidence of moderate quality indicated that compared to bleaching a greater esthetic improvement was seen with resin infiltration (MD=3.6; 95% CI=2.7 to 4.6) or a combination of bleaching with resin infiltration (MD=3.5; 2.8 to 3.7). However, all comparisons were supported from single trials and therefore caution is warranted.

Conclusions: Based on the existing limited evidence, resin infiltration seems to be the most promising treatment for dental fluorosis, followed by bleaching and microabrasion.

TEXT

1 | INTRODUCTION

1.1 | Rationale

Dental fluorosis is a specific esthetic disturbance, which can be described as a chronic condition, where enamel development is disrupted and the resulting enamel is hypomineralized.[1] Concurrent with the worldwide decline of caries, the prevalence of enamel fluorosis has increased in the last two decades.[2,3] This can be explained by an excess of ingested fluoride originating from caries prevention measures like toothpastes, mouthrinses, gels, or varnishes that is incorporated in the enamel during tooth development. This leads to a disturbed enamel formation,[4] as fluoride reduces calcium ion concentration in the matrix, thus indirectly interfering with protease activity and delaying or inhibiting enamel matrix protein degradation.[1,5] An abnormal growth of apatite crystals is seen, which has as consequences optical and physical tooth surface changes.[6]

Optically, dental fluorosis is characterized by hypomineralization of tooth enamel, seen as diffuse, symmetrical, discolored white opaque stains and striations.[1] Enamel surface lesions, such as pitting, porosity, and brownish areas often occur in the more severe forms of fluorosis.[1] Depending on the amount of fluoride uptake, duration of fluoride exposure, and stage of amelogenesis the severity of symptoms varies and requires different measures.[7]

Even though the esthetic perception of enamel mottling is variable across patients, this may have considerable psychosocial effects on many patients and impact their quality of life.[7,8] Therefore, considerable efforts have been put in identifying an effective means to treat fluorotic stains that might be chosen according to lesion severity.[1,9] A wide range of interventions of varying invasiveness have been proposed to treat fluorotic enamel, including external bleaching, microabrasion, dental veneers, or crowns[2,10] or a combination of methods.[11,12] Since patients with enamel mottling are quite young, with a life expectancy of many decades, minimal-invasive, hard-

tissue sparing restorative approaches, such as microabrasion, external bleaching, or resin infiltration have gained momentum.[3,9] Microabrasion is based on the application of an etching gel (mostly HCl) followed by pumicing with slow rotation handpiece. Bleaching of vital fluorotic teeth with various kinds of acids (mostly H_2O_2) that produces peroxide ions to penetrate enamel and dental tubules and reduce the contrast between white spotted lesions and sound enamel have also been widely used. Finally, enamel infiltration with low-viscosity light-cured resins was initially developed to inhibit incipient caries lesions, but has been applied recently in the masking of fluorotic stains, due to the resin's similar to enamel refractive index.

1.2 | Objectives

Although several treatment approaches have been suggested for the treatment of dental fluorosis, their effectiveness has not yet been compared in an evidence-based fashion in order to formulate clinical recommendations. Aim of the present systematic review was to identify and synthesize according to the guidelines of evidence-based medicine all existing evidence from randomized clinical trials in human patients of any age or sex with enamel fluorosis lesions being treated with at least one intervention in any clinical setting.

2 | MATERIALS AND METHODS

2.1 | Protocol and registration

A review protocol was made *a priori* based on the PRISMA-P statement,[13] registered in PROSPERO (CRD42016053492), and all *post hoc* changes were appropriately noted. This systematic review was conducted and reported according to Cochrane Handbook[14] and PRISMA statement,[15] respectively.

2.2 | Eligibility criteria

According to the Participants-Intervention-Comparison-Outcomes-Study design schema (PICOS), we included only randomized controlled trials on humans reporting in vivo any kind of intervention to treat dental fluorosis. Any animal studies, case reports, ongoing trials, non-randomized trials, trials without available full text, or non-relevant trials were excluded.

2.3 | Information sources and literature search

Literature search was carried out systematically by one author (SNP) in nine electronic, general, open access, regional, and grey bibliographic databases, from inception up to December 15th, 2016 (Appendix S1). Additionally, four other sources (Directory of Open Access Journals (DOAJ), Digital Dissertations, metaRegister of Controlled Trials, WHO trials search portal, and Google Scholar) were screened manually for any additional trials. No search filters were applied other than dentistry and trials on humans, where available. The reference lists and citation lists of included trials and relevant reviews were manually searched as well.

2.4 | Study selection

For calibration a pilot study was conducted prior to the main study selection. Subsequently the title, abstract, and full-text of identified studies were screened by one author (TDG) with a subsequent duplicate independent checking for eligibility by a second author (SNP), while conflicts were resolved by a third author (TE). All trials that were not excluded for any of the abovementioned reasons were finally included in our review.

2.5 | Data collection

Characteristics of included trials and numerical data were extracted independently by two review authors (TDG, SNP) using predetermined and piloted extraction forms. Piloting of the forms was performed during the protocol stage until over 90 per cent agreement was reached. Missing or

unclear information was requested from the trial's authors or re-analyzed first-hand, when possible.

2.6 | Risk of bias in individual trials

The risk of bias of included trials was assessed using Cochrane's risk of bias tool[14] after initial calibration.

2.7 | Data synthesis

Meta-analysis was planned to be performed, if similar interventions and control groups were compared and similar outcomes were measured from at least two outcomes with MDs and RRs for continuous and binary outcomes, respectively, and the corresponding 95% Confidence Intervals (CIs). As no two trials on the same comparison were available for meta-analysis, the MDs/RRs were calculated for all included trials and data synthesis was performed descriptively according to the trial's risk of bias and the results' clinical relevance. A clinically relevant effect was conventionally judged as an MD larger than half a standard deviation of the control response or an RR larger than 1.30 (or smaller than 0.70). The overall quality of evidence was rated as very low, low, moderate, or high using the GRADE approach[16] by one author (SNP) and checked by another (TD). The full study dataset was openly provided through Zenodo.[17]

2.8 | Risk of bias across studies and additional analyses

A number of additional analyses and sensitivity analyses for meta-analysis were planned during the protocol stage, but could ultimately not be performed, as no meta-analysis was conducted.

3 | Results

3.1 | Study selection

A total of 572 papers were identified through the electronic and one through manual searches, respectively (Figure 1). After removal of duplicates and initial screening 28 papers were assessed for eligibility, from which six could be included in our review (Appendix S2).

3.2 | Study characteristics

The characteristics of the included papers can be seen in Table 1 and 2. All of the six studies were randomized controlled trials from four countries, with 2 (33%) being within-persons randomized trials and 4 (67%) being parallel randomized trials. A total of 348 patients were included, (with 40% male and 60% female patients in the 4 trials that specified sex) and an average age of 17.7 years (in the 3 trials that specified age). At least 1518 teeth with fluorotic enamel were included, which were treated mostly for esthetic reasons. Fluorosis severity was assessed in two trials with the Thylstrup-Fejerskov index, in one with the Tooth Surface Index of Fluorosis, and in another two with Dean's index, whereas in one trial no fluorosis index was reported. Overall, the identified trials included mild forms of fluorosis, reaching from questionable to moderate fluorosis. Interventions used in the identified trials included external bleaching, microabrasion, resin infiltration with different application times, or combination of bleaching with subsequent resin infiltration. The included trials assessed in all cases efficacy of treatment (esthetic improvement or specific optical properties of the fluorotic lesions), while four of them also assessed safety (tooth sensitivity or irritation of the gingiva) with an outcome measurement timing ranging from directly post-treatment up to six months post-treatment.

3.3 | Risk of bias within studies

The risk of bias assessment for the included six trials is shown in Figure 2 and can be seen more detailed in Appendix S3. Serious risk of bias was found in 4 of the trials (67%) for at least one bias domain, with the most problematic domain being the blinding of outcome assessors (high

risk of bias in 67% of trials), followed by blinding of participants/personnel (high risk of bias in 50% of trials).

3.4 | Results of individual studies and data synthesis

The treatment effects of all outcomes reported in the identified trials can be seen in Appendix S4. Compared to no treatment, bleaching improved all colorimetric aspects according to the International Commission on Illumination to a statistically and clinically significant extent. Although fewer bleached fluorotic areas tended to have discernable color differences from healthy enamel (RR=0.68; 95% CI=0.43 to 1.08), this did not reach statistical significance (P=0.04). The quality of contributing evidence according to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach was judged as low, due to bias and imprecision (Table 3).

As far as direct comparisons between interventions are concerned, bleaching was adopted as a reference intervention, since it contributed with the largest numbers of trials (Table 4). Compared to bleaching, microabrasion resulted in a significantly smaller esthetic improvement of fluorotic stains 6 months after treatment, which was clinically relevant (MD=-2.9; 95% CI=-3.4 to -2.5). On the other side, no difference could be found post treatment in tooth sensitivity between the microabrasion and bleaching. Both conclusions were however supported by evidence of low quality according to GRADE, due to high risk of bias and imprecision (Table 4).

Furthermore, compared to bleaching, all other tested interventions, including resin infiltration for 2', resin infiltration for 3', or bleaching followed by resin infiltration for 3' lead to both statistically and clinically greater esthetic improvements and greater improvements of the fluorotic stains. This was supported by evidence of moderate quality according to GRADE, due to the inclusion of a single trial with limited sample size (as in all cases). Finally, the esthetic improvement was similar for all three listed interventions (MDs of 3.6, 3.6, and 3.5), which

indicated that increased times of resin infiltration (3' instead of 2') or combination with tooth bleaching might not lead to better results.

3.5 | Risk of bias across studies and additional analyses

A number of additional analyses and sensitivity analyses for meta-analysis were planned during the protocol stage, but could ultimately not be performed, as no meta-analysis was conducted.

4 | Discussion

The present systematic review summarizes clinical evidence from six available randomized clinical trials on the treatment of mild to moderate dental fluorosis. According to evidence of low quality, bleaching is effective in significantly improving the colorimetric properties of fluorosed enamel ($P<0.001$; Appendix S4), although the discernable overall color difference between bleached fluorotic and healthy enamel is not significantly different ($P=0.10$; Appendix S4). Additionally, compared to bleaching, microabrasion seems to be associated with smaller esthetic improvement, while resin infiltration for 2' or 3' and bleaching combined with resin infiltration seem to be associated with greater esthetic improvements ($P<0.001$; Appendix S4).

As far as different interventions are compared, microabrasion was found to be significantly less effective in the treatment of fluorotic enamel stains than McInnes bleaching (with a solution of H_2O_2, HCl, and ether). Microabrasion has previously been suggested as an effective means to remove enamel stains that are confined to superficial enamel layers, with possible underlying mechanisms being a dissolution of the residual organic material (including pigmentations) and loosely mineralized tissue by acids, allowing for a subsequent 'correct' remineralization by salivary and fluoride minerals.[3] Others report that it is difficult to determine which stains are sufficiently superficial for correction with microabrasion.[18] Additionally, there are reports that microabrasion might be effective in removing mild fluorotic stains, but might be less effective against fluorotic

stains of even moderate severity.[19] Furthermore, an identified trial that was not included in the GRADE analysis[11] compared microabrasion alone and microabrasion followed by home bleaching, but found no added value from subsequent bleaching.

Additionally, resin infiltration with recommended application strategy (2') or with increased time of infiltrant application (3') showed better results than bleaching in treating fluorotic enamel stains.[12] This might be expected, since resin infiltration has been previously suggested for the treatment of post-orthodontic white spot lesions,[20,21] which have many histological and optical similarities to enamel fluorotic stains.[22,23]

As far as adverse effects are concerned, only a very mild transient tooth sensitivity was recorded after the use of either microabrasion[3,11] or bleaching,[3,11] which was not clinically relevant and subsided after about a month. Additionally, signs of minimal gingival irritation were observed after microabrasion[11] or microabrasion combined with bleaching,[11] which were however transient.

However, some limitations are also present in this study. First and foremost, this systematic review included mostly small trials with limited samples, which can influence their results.[24] Moreover, the limited number of included trials precluded robust assessments of heterogeneity, subgroup analyses for many factors (including tooth type, fluorosis severity, and operator's experience), small-study effects, and reporting biases for all outcomes. Although publication bias could not be tested statistically due to the small number of included studies, we rate the possibility of publication bias as low due to our comprehensive literature screening that included grey literature.

5 | CONCLUSIONS

According to existing evidence from randomized clinical trials in humans, resin infiltration seems to be more effective in the esthetic treatment of mild to moderate fluorotic enamel stains than bleaching and microabrasion. Additionally, no additional gains were found compared to conventional resin infiltration by increased application time of the etchant on enamel or

combination with bleaching. Finally, no serious safety concerns were observed for any of the assessed interventions. However, caution is warranted due to the limited available evidence with moderate to high risk of bias.

REFERENCES

1. Fejerskov, O., Manji, F. & Baelum, V. The nature and mechanisms of dental fluorosis in man. *J. Dent. Res.* **69 Spec No**, 692–700 (1990).
2. Aoba, T. & Fejerskov, O. Dental fluorosis: chemistry and biology. *J. Clin. Epidemiol.* **13**, 155–170 (2002).
3. Bharath, K. et al. Comparison of relative efficacy of two techniques of enamel stain removal on fluorosed teeth. An in vivo study. *J. Clin. Pediatr. Dent.* **38**, 207–213 (2014).
4. Bronckers, A. L., Lyaruu, D. M. & DenBesten, P. K. The impact of fluoride on ameloblasts and the mechanisms of enamel fluorosis. *J. Dent. Res.* **88**, 877–893 (2009).
5. Robinson, C. et al. The effect of fluoride on the developing tooth. *Caries Res*. **38**, 268–276 (2004).
6. Ng, F. & Manton, D. Aesthetic management of severely fluorosed incisors in an adolescent female. *Aust. Dent. J*. **52**, 243–248 (2007).
7. Bertassoni, L. E. et al. In-office dental bleaching and enamel microabrasion for fluorosis treatment. *J. Clin. Pediatr. Dent.* **32**, 185–187 (2008).
8. Celik, E. U., Yildiz, G. & Yazkan, B. Clinical evaluation of enamel microabrasion for the aesthetic management of mild-to-severe dental fluorosis. *J. Esthet. Restor. Dent.* **25**, 422–430 (2013).
9. Khandelwal, V. et al. Aesthetic management of dental fluorosis. *BMJ. Case Rep*. 2013 (2013).
10. Akpata, E. S. Occurrence and management of dental fluorosis. *Int. Dent. J.* **51**, 325–333 (2001).
11. Castro, K. S., et al. Acceptability, efficacy and safety of two treatment protocols for dental fluorosis: A randomized clinical trial. *J. Dent.* **42**, 938–944 (2014).

12. Gugnani, N. et al. Comparative evaluation of esthetic changes in nonpitted fluorosis stains when treated with resin infiltration, in-office bleaching, and combination therapies. *J. Esthet. Restor. Dent.* **29**, 317–324 (2017).

13. Moher, D. et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst. Rev.* **4**, 1 (2015).

14. Higgins, J. & Green, S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [Internet]. The Cochrane Collaboration, 2011. Available from: www.cochrane-handbook.org. Date accessed September 19, 2017.

15. Liberati, A. et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. **339**, b2700 (2009).

16. Guyatt, G. H. et al. GRADE guidelines: A new series of articles in the J Clin Epidemiol. *J. Clin. Epidemiol.* **64**, 380–382 (2011).

17. DiGiovani, T., Eliades, T. & Papageorgiou, S. N. Interventions for dental fluorosis: a systematic review. http://doi.org/10.5281/zenodo.1213781

18. Croll, T. P. & Cavanaugh, R. R. Enamel color modification by controlled hydrochloric acid-pumice abrasion. I. Technique and examples. *Quintessence Int.* **17**, 81–87 (1986).

19. Train, T. E. et al. Examination of esthetic improvement and surface alteration following microabrasion in fluorotic human incisors in vivo. *Pediatr. Dent.* **18**, 353–362 (1996).

20. Paris, S. & Meyer-Lueckel, H. Masking of labial enamel white spot lesions by resin infiltration: a clinical report. *Quintessence Int.* **40**, 713–718 (2009).

21. Höchli, D. et al. Interventions for orthodontically induced white spot lesions: a systematic review and meta-analysis. *Eur. J. Orthod.* **39**,122–133 (2017).

22. Ontiveros, J. C. Commentary: alternative esthetic management of fluorosis and hypoplasia stains: blending effect obtained with resin infiltration techniques. *J. Esthet. Restor. Dent.* **25**, 40–41 (2013).

23. Torres, C. R. & Borges, A. B. Color masking of developmental enamel defects: a case series. *Operative Dent*. **40**, 25–33 (2015).

24. Cappelleri, J. C. et al. Large trials vs meta-analysis of smaller trials: how do their results compare? *JAMA*. **276**, :1332–1338 (1996).

Figure legends

Figure 1 Flow diagram for the identification and selection of eligible trials.

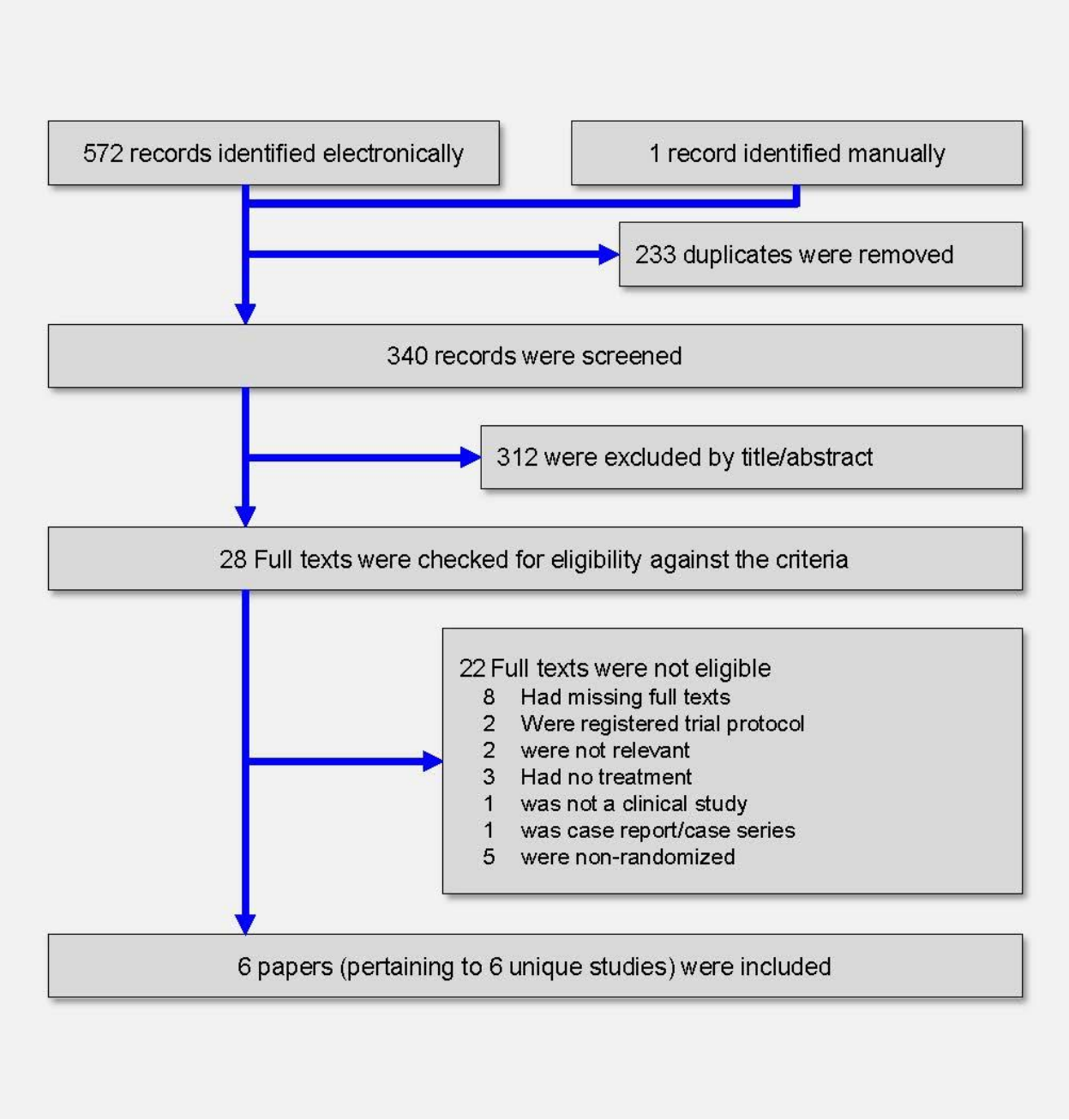

Figure 2 Summary of the risk of bias of included trials.

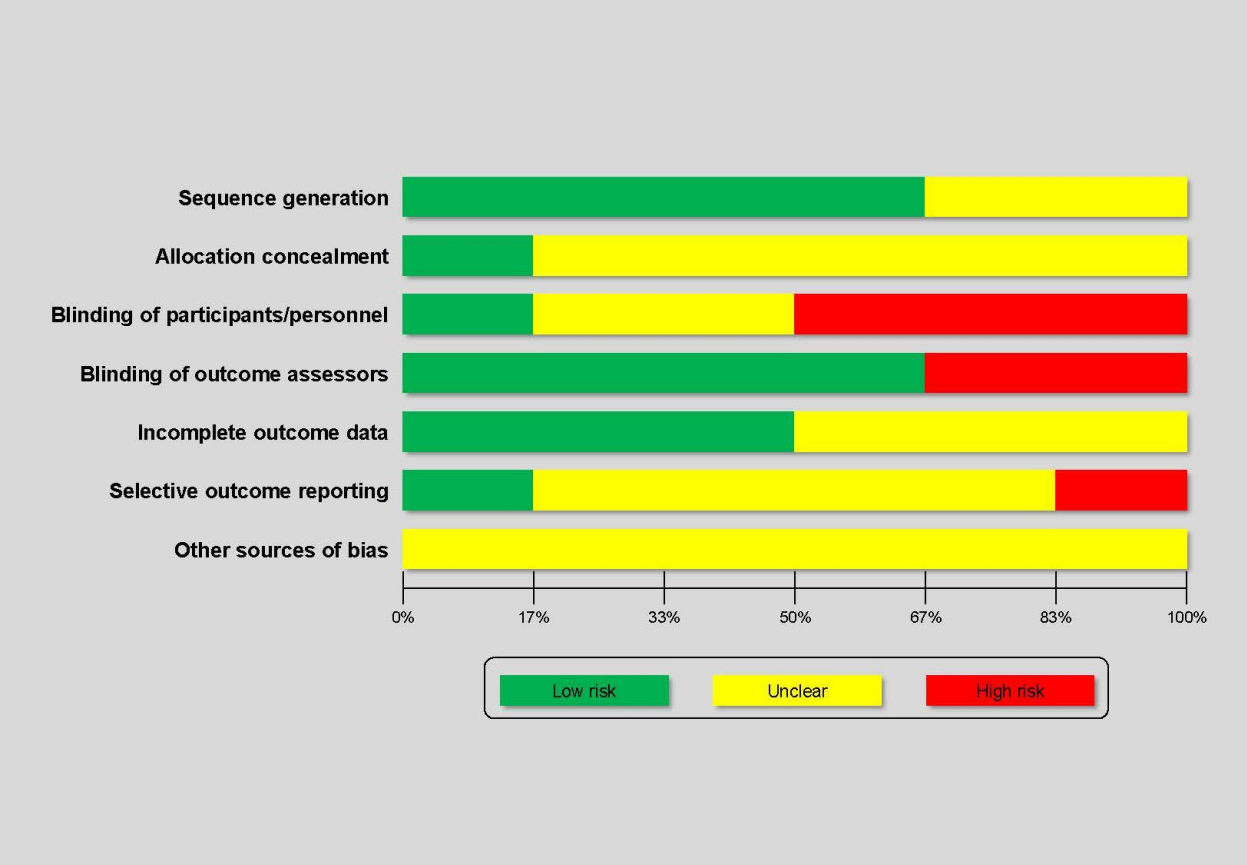

Table 1. Study design and patient characteristics of included trials

Study	Study design; setting; Country	Patients (M/F); age[a]	Patient info	N of teeth	Tooth info Fluorosis index; fluorosis severity; status
Bharath 2014	wpRCT; Uni; IND	30 (NR); 9-14 yrs	objectionable esthetics	60	DFI; mild, moderate; caries-free
Castro 2014	pRCT; Uni; BRA	70 (22/48); 17.6 yrs	>15 yrs, good general/oral health, non-smoker, not pregnant	>280	TF; mild, moderate; vital, caries-, defect-, fracture-, malocclusion-free, restorations less than 1/6 of buccal Sf; orthodontic Tx
Gugnani 2017	pRCT; Uni; IND	80 (NR); 6-12 yrs	School children, good general/oral health, no history of allergy towards dental material	80	TF; mild, moderate; nonpitted, fracture-, restoration-free
Knosel 2008	pRCT; Uni; DEU	18 (7/11); 18.4 yrs	>14 yrs, Caucasian, good oral health	42	NR; mild, moderate; proximal caries-free, sufficient restorations
Loguercio 2007	wpRCT; Uni; BRA	36 (19/17); 10-12 yrs	moderate-good oral health	>144	DFI; questionable, very mild, mild
Loyola-Rodriguez 2003	pRCT; Uni; MEX	114 (40/74); 17.6 yrs	good oral health, no bleaching experience, no history of dental trauma	912	TSIF; <2/3 of tooth surface; caries-, restoration-free, tetracycline-stained-free, intact enamel

[a] when one value is given, this pertains to mean patient age; when this is not reported in the trial, the age range is given.
DFI Dean's Fluorosis Index, *FU* follow-up after treatment administration, *GH* general health, *Gp* group*, M/F mean/female, NR* not reported, *pRCT* parallel randomized clinical trial, *Sf* surface*, smRCT* split-mouth randomized clinical trial, *TF* Thylstrup and Fejerskov Index*, Tx* treatment*, Uni* university*, wpRCT* within-persons randomized clinical trial*, yrs* years.

Table 2. Intervention and outcome characteristics of included trials

Study	Tx; Application time; Application frequency	FU	Outcome
Bharath 2014	Gp1: McInnes Bleaching (36% HCL, 30% H_2O_2, Diethyle Ether); <5 min; NR Gp2: enamel microabrasion (18% HCL, pumice powder); <75 sec; <12-15	1, 3, 6 mos	-esthetic improvement in VAS -tooth sensitivity
Castro 2014	Gp1: enamel microabrasion (37% phosphoric acid, pumice); (n=23) 4 min, (n=12) 2 min; (n=23) 24, (n=12) 12 Gp2: enamel microabrasion (37% phosphoric acid, pumice), at-home bleaching (10% carbamide peroxide); (n=22) 56 h 4 min, (n=13) 56 h 2 min; (n=22) 38 (n=13) 26	1 mos	-reduction in opacity with software -esthetic improvement in VAS -participant satisfaction in VAS -tooth sensitivity/gingiva irritation in VAS
Gugnani 2017	Gp1: in-office bleaching (35% H_2O_2); 8 min; 1 Gp2: resin infiltration (15% HCL gel, ethanol-drying agent, resin infiltrant); <10 min; 1 Gp3: resin infiltration with double application of infiltrant; <12 min; 1 Gp4: in-office bleaching (35% H_2O_2), resin infiltration; <18 min; 1	Immedi-ately	- esthetic change in VAS - improvement in opacity/stains in VAS
Knosel 2008	Gp1: external bleaching Illuminé office (30% hydrogen peroxide), Illuminé home (15% carbamide peroxide); 15 h; 15 Gp2: control	1 h; 14 d; 28 d	-tooth color, luminosity (colorimetry) - tooth sensitivity, enamel surface, gingival irritation in questionnaire -participant satisfaction in question-naire
Loguercio 2007	Gp1: enamel microabrasion PREMA; 10 min; 15 Gp2: enamel microabrasion Opalustre; 10 min; 15	NR	-esthetic improvement in VAS -participant satisfaction -tooth surface
Loyola-Rodri-guez 2003	Gp1: external bleaching (10% carbamide peroxide); 56 h; 7 Gp2: external bleaching (20% carbamide peroxide); 56 h; 7 Gp3: external bleaching (7.5% hydrogen peroxide); 56 h; 7	7 d	-esthetic improvement -tooth sensitivity -gingiva irritation

FU follow-up after treatment administration, *GH* general health, *Gp* group, *M/F* mean/female, *min* minutes, *mos* months, *NR* not reported, *OH* oral health, *sec* seconds, *Sf* surface, *TF* Thylstrup and Fejerskov Index, *TSIF* Tooth Surface Index of Fluorosis, *Tx* treatment, *Uni* university, *yrs* years.

Table 3. GRADE Summary of Findings Table for meta-analyses of trials comparing bleaching to no treatment for fluorosed enamel

	Anticipated absolute effects					
Outcome Trials (patients) – follow up	**Effect (95% CI)**	**Control***	**Bleaching**	**Difference**	**Quality of the evidence (GRADE)[a]**	**What happens**
ΔE(L*a*b*) >3.7 between fluorosed and healthy enamel 1 (18) – 1 month post Tx	RR: 0.68 (0.43,1.08)	76.5%	52.0% (32.9%,82.6%)	24.5% less (43.6% less, 6.1% more)	⊕⊕◯◯ low[b,c] due to bias, imprecision	Bleaching might make fluorotic enamel less discernable

CI confidence interval, *GRADE* Grading of Recommendations Assessment, Development and Evaluation, *RR* relative risk, *Tx* treatment, *ΔE(L*a*b)* overall color difference according to the International Commission on Illumination.

Treatment effects of interventions for enamel fluorosis.

Patient or population: Caucasian male & female adolescent/adult patients seeking treatment for fluorotic stains on teeth.

Settings: university clinics (Germany).

* Risk in the control group is based on the untreated control group of the single included study.

[a] Quality of evidence starts from high due to the inclusion of randomized studies.

[b] Downgraded by one due to risk of bias.

[c] Downgraded by one due to imprecision originating from the inclusion of a single study with limited sample size.

Table 4. GRADE Summary of Findings Table for meta-analyses of trials comparing bleaching to different treatments for fluorosed enamel

	Anticipated absolute effects				
Outcome Trials (patients) – follow up	**Ref (BLCH)***	**Experi-mental**	**Difference (95% CI)**	**Quality of the evidence (GRADE)[a]**	**What happens (with reference to bleaching)**
		MABR			
Esthetic improvement 1(30) – 6 months post Tx	+5.8 VAS_{1-7} pts improvement	-	MD: 2.9 pts less (2.5 to 3.4 pts less)	⊕⊕◯◯ low[b,c] due to bias, imprecision	Smaller esthetic improvement with microabrasion
Tooth sensitivity 1(30) – post Tx	0.4 pts in SS_{0-3}	-	MD: 0.1 pts less (0.4 pts less to 0.2 pts more)	⊕⊕◯◯ low[b,c] due to bias, imprecision	Probably no difference in tooth sensitivity.
		RESINF (2')			
Esthetic improvement 1(40) – post Tx	+1.9 VAS_{1-7}pts improvement	-	MD: 3.6 pts more (3.0 to 4.2 pts more)	⊕⊕⊕◯ moderate[c] due to imprecision	Greater esthetic improvement with resin infiltration (2').
Improvement of fluorosis stains 1 (40) – post Tx	+1.5 VAS_{1-7}pts improvement	-	MD: 3.5 pts more (2.8 to 4.1 pts more)	⊕⊕⊕◯ moderate[c] due to imprecision	Greater improvement of stains with resin infiltration (2').
		RESINF (3')			
Esthetic improvement 1(40) – post Tx	+1.9 VAS_{1-7}pts improvement	-	MD: 3.6 pts more (2.7 to 4.6 pts more)	⊕⊕⊕◯ moderate[c] due to imprecision	Greater esthetic improvement with resin infiltration (3').
Improvement of fluorosis stains 1 (40) – post Tx	+1.5 VAS_{1-7}pts improvement	-	MD: 3.7 pts more (2.9 to 4.4 pts more)	⊕⊕⊕◯ moderate[c] due to imprecision	Greater improvement of stains with resin infiltration (3').
		BLCH & RESINF (3')			
Esthetic improvement 1(40) – post Tx	+1.9 VAS_{1-7}pts improvement	-	MD: 3.5 pts more (2.8 to 3.7 pts more)	⊕⊕⊕◯ moderate[c] due to imprecision	Greater esthetic improvement with bleaching + resin infiltration (3').

BLCH bleaching, *CI* confidence interval, *GRADE* Grading of Recommendations Assessment, Development and Evaluation, *MABR* microabrasion, *MD* mean difference, *pts* points, *Ref* referent intervention, *RESINF* resinfiltration (infiltration time indicated in parenthesis), SS_{0-3} sensitivity scale from 0 to 3 (greater values indicated greater tooth sensitivity), *Tx* treatment, VAS_{1-7} visual analogue scale from 1 to 7 (greater values indicated greater improvement).
Treatment effects of interventions for enamel fluorosis.
Patient or population: children with mild to moderate non-pitted fluorotic stains on teeth receiving treatment.
Settings: dental college (India).
* Reponse in the reference group is based on the single included study in each comparison.
[a] Quality of evidence starts from high due to the inclusion of randomized studies.
[b] Downgraded by one due to risk of bias.
[c] Downgraded by one due to imprecision originating from the inclusion of a single study with limited sample size.

Interventions for dental fluorosis: a systematic review

Supporting Information

Appendix S1. Literature databases searched with the used search strategies and their hits (search date December 20, 2016)

Nr	Database	Search	Limit	Hits
1	MEDLINE (via PubMed) https://www.ncbi.nlm.nih.gov/pubmed/	(dent* OR teeth OR tooth) AND (fluorosis OR fluorosed OR fluorozed OR mottl*) AND random*	Species: Human	156
2	Cochrane Database of Systematic Reviews (CDSR) http://cochranelibrary.com/	(dent* OR teeth OR tooth) AND (fluorosis OR fluorosed OR fluorozed OR mottl*)	-	5
3	Cochrane Central Register of Controlled Trials (CENTRAL) http://cochranelibrary.com/	(dent* OR teeth OR tooth) AND (fluorosis OR fluorosed OR fluorozed OR mottl*)	-	65
4	Cochrane Database of Abstracts of Reviews of Effects (DARE) http://cochranelibrary.com/	(dent* OR teeth OR tooth) AND (fluorosis OR fluorosed OR fluorozed OR mottl*)	-	7
5	Embase https://embase.com/	(dent* OR teeth OR tooth) AND (fluorosis OR fluorosed OR fluorozed OR mottl*) AND random*	Human	95
6	Virtual Health Library http://bvsalud.org/en/	(dent* OR teeth OR tooth) AND (fluorosis OR fluorosed OR fluorozed OR mottl*) AND random*	-	49
7	Scopus https://scopus.com/	(dent* OR teeth OR tooth) AND (fluorosis OR fluorosed OR fluorozed OR mottl*) AND random*	Dentistry; Human	98
8	Web of Knowledge https://login.webofknowledge.com/	(dent* OR teeth OR tooth) AND (fluorosis OR fluorosed OR fluorozed OR mottl*) AND random*	DENTISTRY ORAL SURGERY MEDICINE	89
9	ClinicalTrials.gov https://clinicaltrials.gov/	(dental OR dentistry OR teeth OR tooth) AND (fluorosis OR fluorosed OR fluorozed OR mottled OR mottling)		8
SUM				572

.

Appendix S2. List of identified studies with eligibility status.

Nr	Paper	Status
1	[No authors] A systematic review of public water fluoridation. Database of Abstracts of Reviews of Effects. 2000; 2:243.	Excluded by title
2	{NCT01049503} Effect of pH and Fluoride Concentration of Dentifrices on Caries Control. Completed.	Excluded by title
3	{NCT01568541} Fluoride Intake From Toothbrushig With Children's or Regular Toothpastes. Completed.	Excluded by title
4	{NCT01571050} Systemic Fluoride Bioavailability From Toothpastes Containing Calcium Carbonate or Silica as Abrasives. Completed.	Excluded by title
5	{NCT01589991} Anticaries Potential and Fluorosis Risk From Different Fluoride Toothpastes. Completed	Excluded by title
6	{NCT01978041} Fluoride Bioavailability After Ingestion of Water or Foods Prepared With Fluoridated Water. Completed.	Excluded by title
7	{NCT02958891} Dental Health Epidemiology Among Israel Defense Forces (IDF) Recruits. Active, not recruiting.	Excluded by title
8	Aasenden R, Peebles T. Effects of fluoride supplementation from birth on dental caries and fluorosis in teenaged children. Archives of oral biology. 1978; 23(2):[111-5 pp.].	Excluded by title
9	Abuhaloob L, Abed Y. Dietary behaviours and dental fluorosis among Gaza Strip children. Eastern Mediterranean health journal = La revue de sante de la Mediterranee orientale = al-Majallah al-sihhiyah li-sharq al-mutawassit. 2013;19(7):657-63.	Excluded by title
10	Adair SM, Piscitelli WP, McKnight-Hanes C. Comparison of the use of a child and an adult dentifrice by a sample of preschool children. Pediatric dentistry. 1997;19(2):99-103.	Excluded by title
11	Ahiropoulos V. Fluoride content of bottled waters available in Northern Greece. International journal of paediatric dentistry. 2006;16(2):111-6.	Excluded by title
12	Ajayi DM, Arigbede AO, Dosumu OO, Ufomata D. The prevalence and severity of dental fluorosis among secondary school children in Ibadan, Nigeria. The Nigerian postgraduate medical journal. 2012;19(2):102-6.	Excluded by title
13	Akosu TJ, Zoakah AI, Chirdan OA. The prevalence and severity of dental fluorosis in the high and low altitude parts of Central Plateau, Nigeria. Community dental health. 2009;26(3):138-42.	Excluded by title
14	Akosu TJ, Zoakah AI. Risk factors associated with dental fluorosis in Central Plateau State, Nigeria. Community dentistry and oral epidemiology. 2008;36(2):144-8.	Excluded by title
15	Akpata ES, Behbehani J, Akbar J, Thalib L, Mojiminiyi O. Fluoride intake from fluids and urinary fluoride excretion by young children in Kuwait: a non-fluoridated community. Community dentistry and oral epidemiology. 2014;42(3):224-33.	Excluded by title
16	Al Agili DE, Alaki SM. Can Socioeconomic Status Indicators Predict Caries Risk in Schoolchildren in Saudi Arabia? A Cross-sectional Study. Oral health & preventive dentistry. 2014;12(3):277-88.	Excluded by title
17	al-Khateeb TL, Darwish SK, Bastawi AE, O'Mullane DM. Dental caries in children residing in communities in Saudi Arabia with differing levels of natural fluoride in the drinking water. Community dental health. 1990;7(2):165-71.	Excluded by title
18	Allmark C, Green H, Linney A, Wills D, Picton D. A community study of fluoride tablets for school children in Portsmouth: results after six years. British dental journal. 1982; 153(12).	Excluded by title
19	Al-Mobeeriek AF, Al-Shamrani SM, Al-Hussyeen AJA, Bushnaq HZ, Al-Waheib RA. Knowledge and attitude of dental health workers towards fluoride in Riyadh area. Saudi Medical Journal. 2001;22(11):1004-7.	Excluded by title
20	Amaral JG, Freire IR, Valle-Neto EFR, Cunha RF, Martinhon CCR, Delbem ACB. Longitudinal evaluation of fluoride levels in nails of 18-30-month-old children that were using toothpastes with 500 and 1100 mu g F/g. Community dentistry and oral epidemiology. 2014;42(5):412-9.	Excluded by title
21	Ammari AB, Bloch-Zupan A, Ashley PF. Systematic review of studies comparing the anti-caries efficacy of children's toothpaste containing 600 ppm of fluoride or less with high fluoride toothpastes of 1,000 ppm or above. Caries research. 2003;37(2):85-92.	Excluded by title
22	An D, He P, Li DS, Yin L, Jin ZJ, Hu XQ. Main fluoride origin of the key regions of coal-burning endemic fluorosis in Guizhou Province. Chinese Journal of Endemiology. 2009;28(6):629-32.	Excluded by title
23	Antony KM, Harris RA, Levison J, Banda B, Chiudzu G, Chirwa R, et al. Population-based estimation of the peridontal disease rate in malawi and compliance with preventive/ treatment measures. American Journal of Obstetrics and Gynecology. 2016;214(1):S295-S6.	Excluded by title
24	Arellano LA, Fleitas AT, Ramírez AC. Prevalencia e intensidad de fluorosis dental en escolares de 10-13 años de edad en San Carlos y Santa Bárbara de Zulia, Venezuela. Acta Odontol Venez. 1998;36(2):102-6.	Excluded by title
25	Arnold F, Dean H, Jay P, Knutson J. Effect of fluoridated public water supplies on dental caries prevalence. 1956. Bulletin of the World Health Organization. 2006; 84(9):[761-4 pp.].	Excluded by title
26	Arrieta-Vergara KM, González-Martínez F, Luna-Ricardo L. Exploración del riesgo para fluorosis dental en niños de las clínicas odontológicas universidad de Cartagena. Rev Salud Publica (Bogota). 2011;13(4):672-83.	Excluded by title
27	Astrom AN, Awadia AK, Bjorvatn K. Perceptions of susceptibility to oral health hazards: a study of women in different cultures. Community dentistry and oral epidemiology. 1999;27(4):268-74.	Excluded by title
28	Azcurra AI, Battellino LJ, Calamari SE, de Cattoni ST, Kremer M, Lamberghini FC. [Dental health status of students living in places supplied with drinking water of very high and very low levels of fluorides]. Revista de saude publica. 1995;29(5):364-75.	Excluded by title
29	Azevedo MS, Goettems ML, Torriani DD, Demarco FF. Factors associated with dental fluorosis in school children in southern Brazil: a cross-sectional study. Brazilian oral research. 2014;28.	Excluded by title
30	Bagramian RA, Narendran S, Ward M. Relationship of dental caries and fluorosis to fluoride supplement history in a non-fluoridated sample of schoolchildren. Advances in dental research. 1989;3(2):161-7.	Excluded by title
31	Bai A, Li Y, Fan Z, Li X, Li P. Intelligence and growth development of children in coal-burning-borne arsenism and fluorosis areas: An investigation study. Chinese Journal of Endemiology. 2014;33(2):160-3.	Excluded by title
32	Bal IS, Dennison PJ, Evans RW. Dental fluorosis in the Blue Mountains and Hawkesbury, New South Wales, Australia: policy implications. Journal of investigative and clinical dentistry. 2015;6(1):45-52.	Excluded by title
33	Baloch HN, Mengal N, Khail AAK, Kurd SA, Alizai KA. Prevalence of fluorosis among children aged 12 years, living in urban peri-urban areas of Quetta District, Balochistan. Medical Forum Monthly. 2013;24(6):30-3.	Excluded by title
34	Bao L, Li Y, Zhang Y. [Dental caries and fluorosis among 12-year-old children with different fluoride exposure in Heilongjiang province]. Shanghai kou qiang yi xue = Shanghai journal of stomatology. 2007;16(6):574-7.	Excluded by title
35	Bardal PAP, Olympio KPK, Buzalaf MAR, Bastos JRdM. Dental caries and dental fluorosis in 7-12-year-old schoolchildren in Catalão, Goiás, Brazil%Cárie e fluorose dentária em escolares de 7 a 12 anos de idade em Catalão, Goiás, Brasil. J appl oral sci. 2005;13(1):35-40.	Excluded by title
36	Bentley EM, Ellwood RP, Davies RM. Fluoride ingestion from toothpaste by young children. British dental journal. 1999;186(9):460-2.	Excluded by title
37	Bijella M, Brighenti F, Bijella M, Buzalaf M. Fluoride kinetics in saliva after the use of a fluoride-containing chewing gum. Brazilian oral research. 2005; 19(4):[256-60 pp.].	Excluded by title

38	Bohaty BS, Parker WA, Seale NS, Zimmerman ER. The prevalence of fluorosis-like lesions associated with topical and systemic fluoride usage in an area of optimal water fluoridation. Pediatric dentistry. 1989;11(2):125-8.	Excluded by title
39	Brighenti FL, Delbem ACB, Buzalaf MAR, Oliveira FAL, Ribeiro DB, Sassaki KT. In vitro evaluation of acidified toothpastes with low fluoride content. Caries research. 2006;40(3):239-44.	Excluded by title
40	Budipramana ES, Hapsoro A, Irmawati ES, Kuntari S. Dental fluorosis and caries prevalence in the fluorosis endemic area of Asembagus, Indonesia. International journal of paediatric dentistry. 2002;12(6):415-22.	Excluded by title
41	Cain BE, Corpron RE, Fee CL, Strachan DS, Kowalski CJ. Dose-Related Remineralization Using Intraoral Fluoride-Releasing Devices in-Situ. Caries research. 1994;28(4):284-90.	Excluded by title
42	Candeli A, Capozzi L, Marci F, Marchini G. The determination of fluoride within the teeth by means of biopsy on the enamel. Caries research. 1967; 1(2).	Excluded by title
43	Cardoso CDAB, Lacerda B, Mangueira DFB, Charone S, Olympio KPK, Magalhães AC, et al. Mechanisms of action of fluoridated acidic liquid dentifrices against dental caries. Archives of oral biology. 2014;60(1):23-8.	Excluded by title
44	Cardoso CdAB. Efeito do pH e da concentração de fluoreto presente em dentifrícios líquidos no controle de cárie em área fluoretada: estudo clínico randomizado. 2013:152-.	Excluded by title
45	Cardoso CDB, Mangueira DFB, Olympio KPK, Magalhaes AC, Rios D, Honorio HM, et al. The effect of pH and fluoride concentration of liquid dentifrices on caries progression. Clinical Oral Investigations. 2014;18(3):761-7.	Excluded by title
46	Cardoso Cde A, Lacerda B, Mangueira DF, Charone S, Olympio KP, Magalhaes AC, et al. Mechanisms of action of fluoridated acidic liquid dentifrices against dental caries. Archives of oral biology. 2015;60(1):23-8.	Excluded by title
47	Carvalho TS, Kehrle HM, Sampaio FC. Prevalence and severity of dental fluorosis among students from Joao Pessoa, PB, Brazil. Brazilian oral research. 2007;21(3):198-203.	Excluded by title
48	Catani DB, Tenuta LMA, Andaló FA, Cury JA. Fluorosis in rats exposed to oscillating chronic fluoride doses. Braz Dent J. 2010;21(1):32-7.	Excluded by title
49	Chandrashekar J, Thankappan KR, Sundaram KR. Severe dental fluorosis and jowar consumption in Karnataka, India. Community dentistry and oral epidemiology. 2010;38(6):559-67.	Excluded by title
50	Chen S, Li B, Lin S, Huang Y, Zhao X, Zhang M, et al. Change of urinary fluoride and bone metabolism indicators in the endemic fluorosis areas of southern China after supplying low fluoride public water. BMC public health. 2013;13:156.	Excluded by title
51	Chiba FY, Gallinari MO, Gomes WDS, Colombo NH, Shirakashi DJ, Sumida DH. The chronic treatment with NaF decreases insulin signal in the muscle but not in the liver. Diabetes. 2010.	Excluded by title
52	Chiba FY. Avaliação da etapa inicial do sinal insulínico em tecido muscular e hepático de ratos tratados cronicamente com NaF. 2010:104-.	Excluded by title
53	Chou R, Cantor A, Zakher B, Mitchell JP, Pappas M. Preventing dental caries in children <5 years: systematic review updating USPSTF recommendation. Pediatrics. 2013;132(2):332-50.	Excluded by title
54	Clerehugh A. Enamel mottling in 15-year-old children in Barnsley Area, England. Community dentistry and oral epidemiology. 1979;7(6):349-52.	Excluded by title
55	Cochran JA, Ketley CE, Arnadottir IB, Fernandes B, Koletsi-Kounari H, Oila AM, et al. A comparison of the prevalence of fluorosis in 8-year-old children from seven European study sites using a standardized methodology. Community dentistry and oral epidemiology. 2004;32 Suppl 1:28-33.	Excluded by title
56	Cochran JA, Ketley CE, Duckworth RM, van Loveren C, Holbrook WP, Seppa L, et al. Development of a standardized method for comparing fluoride ingested from toothpaste by 1.5-3.5-year-old children in seven European countries. Part 2: Ingestion results. Community dentistry and oral epidemiology. 2004;32 Suppl 1:47-53.	Excluded by title
57	Conway DI, MacPherson LM, Stephen KW, Gilmour WH, Petersson LG. Prevalence of dental fluorosis in children from non-water-fluoridated Halmstad, Sweden: fluoride toothpaste use in infancy. Acta odontologica Scandinavica. 2005;63(1):56-63.	Excluded by title
58	Cury J, Fiol F, Tenuta L, Rosalen P. Low-fluoride dentifrice and gastrointestinal fluoride absorption after meals. Journal of dental research. 2005; 84(12):[1133-7 pp.].	Excluded by title
59	Cypriano S, Pecharki GD, de Sousa Mda L, Wada RS. [Oral health of schoolchildren residing in areas with or without water fluoridation in Sorocaba, Sao Paulo State, Brazil]. Cadernos de saude publica. 2003;19(4):1063-71.	Excluded by title
60	Delbem AC, Bergamaschi M, Rodrigues E, Sassaki KT, Vieira AE, Missel EM. Anticaries effect of dentifrices with calcium citrate and sodium trimetaphosphate. Journal of applied oral science : revista FOB. 2012;20(1):94-8.	Excluded by title
61	DenBesten P, Ko HS. Fluoride levels in whole saliva of preschool children after brushing with 0.25 g (pea-sized) as compared to 1.0 g (full-brush) of a fluoride dentifrice. Pediatric dentistry. 1996;18(4):277-80.	Excluded by title
62	Deng LY, Zhang YS, Gao JP. Analysis of monitoring results of coal-burning borne endemic fluorosis in Fuyuan county Qujing city in 2009. Chinese Journal of Endemiology. 2012;31(2):205-6.	Excluded by title
63	Desai VK, Bhavsar BS, Mehta NR, Krishnamachari KAVR. Clinical radiological observations among workers of fluoride processing industry. Fluoride - Quarterly Reports. 1983;16(2):90-100.	Excluded by title
64	Detsomboonrat P, Trairatvorakul C, Pisarnturakit PP. Similar 1-year caries increment after use of fluoride or non-fluoride toothpaste in infants and toddlers. Fluoride. 2016;49(3):313-26.	Excluded by title
65	Dhanuthai K, Thangpisityotin M. Fluoride content of commercially-available bottled water in Bangkok, Thailand. Journal of investigative and clinical dentistry. 2011;2(2):144-7.	Excluded by title
66	Dhingra K, Vandana KL, Girish PV, Cobb C. Effect of 980-nm diode laser-aided circumferential supracrestal fiberotomy on fluorosed root surfaces. The Angle orthodontist. 2013;83(3):425-30.	Excluded by title
67	Dhingra S, Marya CM, Jnaneswar A, Kumar H. Fluoride concentration in community water and bottled drinking water: a dilemma today. Kathmandu University medical journal (KUMJ). 2013;11(42):117-20.	Excluded by title
68	Ding Y, YanhuiGao, Sun H, Han H, Wang W, Ji X, et al. The relationships between low levels of urine fluoride on children's intelligence, dental fluorosis in endemic fluorosis areas in Hulunbuir, Inner Mongolia, China. Journal of hazardous materials. 2011;186(2-3):1942-6.	Excluded by title
69	Dini EL, Holt RD, Bedi R. Prevalence of caries and developmental defects of enamel in 9-10 year old children living in areas in Brazil differing water fluoride histories. British dental journal. 2000;188(3):146-9.	Excluded by title
70	Do LG, Ha DH, Spencer AJ. Factors attributable for the prevalence of dental caries in Queensland children. Community dentistry and oral epidemiology. 2015;43(5):397-405.	Excluded by title
71	Do LG, Spencer AJ. Risk-benefit balance in the use of fluoride among young children. Journal of dental research. 2007;86(8):723-8.	Excluded by title
72	Dominguez-Cortinas G, Cifuentes E, Escobar ER, Martinez FD. Assessment of environmental health children's population living in environmental injustice scenarios. Journal of community health. 2012;37(6):1199-207.	Excluded by title
73	Dong Y-N, Chen M, Ren X-M. Effect of fluor protector on preventing enamel demineralization. Journal of Clinical Rehabilitative Tissue Engineering Research. 2009; 13(25):[4997-5000 pp.].	Excluded by title

74	dos Santos APP, Malta MCB, de Marsillac MDS, de Oliveira BH. Fluoride Varnish Applications in Preschoolers and Dental Fluorosis in Permanent Incisors: Results of a Nested-cohort Study Within a Clinical Trial. Pediatric dentistry. 2016;38(5):414-8.	Excluded by title
75	Downer MC, Blinkhorn AS, Holt RD, Wight C, Attwood D. Dental caries experience and defects of dental enamel among 12-year-old children in north London, Edinburgh, Glasgow and Dublin. Community dentistry and oral epidemiology. 1994;22(5 Pt 1):283-5.	Excluded by title
76	Eglash A, Kendall SK. What vitamins and minerals should be given to breastfed and bottle-fed infants? Journal of Family Practice. 2005;54(12):1089-91.	Excluded by title
77	Ekambaram M, Itthagarun A, King NM. Comparison of the remineralizing potential of child formula dentifrices. International journal of paediatric dentistry. 2011;21(2):132-40.	Excluded by title
78	Ekstrand J, Fomon S, Ziegler E, Nelson S. Fluoride pharmacokinetics in infancy. Pediatric research. 1994; 35(2):[157-63 pp.].	Excluded by title
79	Ellwood R, Mullane D. An investigation of tooth brushing behaviour and dental fluorosis in premolars [abstract]. Journal of dental research. 1995; 74(3 [Divisional Abstracts: British Division]).	Excluded by title
80	Falcao A, Tenuta LM, Cury JA. Fluoride gastrointestinal absorption from Na2FPO3/CaCO3- and NaF/SiO2-based toothpastes. Caries research. 2013;47(3):226-33.	Excluded by title
81	Falcão A, Tenuta LMA, Cury JA. Fluoride gastrointestinal absorption from Na<inf>2</inf> FPO <inf>3</inf>/CaCO<inf>3</inf>- and NaF/SiO<inf>2</inf>-Based toothpastes. Caries research. 2013;47(3):226-33.	Excluded by title
82	Fan ZX, Li Y, Li XQ, Bai GL, Li PA, Liu XL, et al. Analysis of monitoring results of coal-burning borne endemic fluorosis in Shanxi province in 2010. Chinese Journal of Endemiology. 2012;31(2):194-8.	Excluded by title
83	Fan ZX, Li Y, Li XQ, Bai GL, Liu XL, Bai AM, et al. Drinking-water type of fluorosis in Shaanxi province in 2009: An analysis of surveillance results. Chinese Journal of Endemiology. 2011;30(3):294-7.	Excluded by title
84	Ferro R, Besostri A, Giuca MR, Docimo R, Gatto R, Marzo G. The Italian perspective on fluoride intake in children and adolescents. European Journal of Paediatric Dentistry. 2014;15(1):55-8.	Excluded by title
85	Firempong C, Nsiah K, Awunyo-Vitor D, Dongsogo J. Soluble fluoride levels in drinking water-a major risk factor of dental fluorosis among children in Bongo community of Ghana. Ghana medical journal. 2013;47(1):16-23.	Excluded by title
86	Forte FD, Freitas CH, Sampaio FC, Jardim MC. [Dental fluorosis in children from Princesa Isabel, Paraiba]. Pesquisa odontologica brasileira = Brazilian oral research. 2001;15(2):87-90.	Excluded by title
87	Gao RP, Xu Y. Analysis of disease surveillance of endemic fluorosis in Yanqing county of Beijing in 2008. Chinese Journal of Endemiology. 2010;29(2):176-8.	Excluded by title
88	García-Camba de la Muela JM, García Hoyos F, Varela Morales M, González Sanz Á. Absorción sistemática de flúor en niños secundaria al cepillado con dentífrico fluorado. Revista espanola de salud publica. 2009;83(3):415-25.	Excluded by title
89	Garcia-Camba de la Muela JM, Garcia-Hoyos F, Varela Morales M, Gonzalez Sanz A. [Demonstration of fluoride systemic absorption secondary to toothbrushing with fluoride dentifrice in children]. Revista espanola de salud publica. 2009;83(3):415-25.	Excluded by title
90	Garcia-Hoyos F, Barberia E, Garcia-Camba P, Varela M. Renal fluoride excretion in children following topical application of fluoride varnish. European Journal of Paediatric Dentistry. 2012;13(4):280-4.	Excluded by title
91	Garcia-Hoyos F, Silva CC, Barberia E. Renal excretion of fluoride after fluoride mouth rinses in children. European Journal of Paediatric Dentistry. 2014;15(1):35-8.	Excluded by title
92	Ge SZG. Analysis of monitoring results of drinking-tea borne endemic fluorosis in Lhasa of Tibet. Chinese Journal of Endemiology. 2012;31(3):325-8.	Excluded by title
93	Gomes PR, Costa SC, Cypriano S, de Sousa Mda L. [Dental caries in Paulinia, Sao Paulo State, Brazil, and WHO goals for 2000 and 2010]. Cadernos de saude publica. 2004;20(3):866-70.	Excluded by title
94	Gómez Soler SS, Fernández A V, Salas V E, Suez V G. Prevalencia y severidad de fluorosis dental atribuible a la ingesta multivehicular de fluoruros. Rev Fac Odontol Univ Valparaiso. 1999;2(3):182-9.	Excluded by title
95	Gonzales C, Hotokezaka H, Karadeniz EI, Miyazaki T, Kobayashi E, Darendeliler MA, et al. Effects of fluoride intake on orthodontic tooth movement and orthodontically induced root resorption. American Journal of Orthodontics and Dentofacial Orthopedics. 2011;139(2):196-205.	Excluded by title
96	Gopalakrishnan P, Vasan RS, Sarma PS, Nair KS, Thankappan KR. Prevalence of dental fluorosis and associated risk factors in Alappuzha district, Kerala. The National medical journal of India. 1999;12(3):99-103.	Excluded by title
97	Goward PE. Enamel mottling in a non-fluoride community in England. Community dentistry and oral epidemiology. 1976;4(3):111-4.	Excluded by title
98	Guerra LM, Pereira AC, Pereira SM, Meneghim MdC. Avaliação de variáveis socioeconômicas na prevalência de cárie e fluorose em municípios com e sem fluoretação das águas de abastecimento. Rev odontol UNESP (Online). 2010;39(5).	Excluded by title
99	Gupta SK, Gupta RC, Seth AK, Chaturvedi CS. Increased incidence of spina bifida occulta in fluorosis prone areas. Acta paediatrica Japonica : Overseas edition. 1995;37(4):503-6.	Excluded by title
100	Gupta SK, Khan TI, Gupta RC, Gupta AB, Gupta KC, Jain P, et al. Compensatory hyperparathyroidism following high fluoride ingestion - A clinico-biochemical correlation. Indian pediatrics. 2001;38(2):139-46.	Excluded by title
101	Haikel Y, Voegel JC, Frank RM. Fluoride content of water, dust, soils and cereals in the endemic dental fluorosis area of Khouribga (Morocco). Archives of oral biology. 1986;31(5):279-86.	Excluded by title
102	Halabi MA. Current guidelines for the use of fluoride in pediatric dentistry, a review. Applied Clinical Research, Clinical Trials and Regulatory Affairs. 2014;1(3):135-44.	Excluded by title
103	Hamdan MA. The prevalence and severity of dental fluorosis among 12-year-old schoolchildren in Jordan. International journal of paediatric dentistry. 2003;13(2):85-92.	Excluded by title
104	Handa S, Prasad S, Rajashekharappa CB, Garg A, Ryana HK, Khurana C. Oral health status of rural and urban population of Gurgaon block, Gurgaon district using WHO assessment form through multistage sampling technique. Journal of Clinical and Diagnostic Research. 2016;10(5):ZC43-ZC451.	Excluded by title
105	Harinath B. An epidemiological study of dental fluorosis among higher secondary school children belonging to an endemic rural area in Nalgonda district, Andhra Pradesh. Australasian Medical Journal. 2012;5(1):42-3.	Excluded by title
106	Hassan AK, Saifi MAB, Najim ZN. Prevalence of dental flourosis in Fazan (South Libya). Journal of the Bahrain Medical Society. 2002;14(3):85-90.	Excluded by title
107	He FZ, Guo M, Danzengsangbu, Nimacangjue, Baimayangjin. Surveillance analysis of drinking water borne fluorosis in Tibet autonomous region in 2009. Chinese Journal of Endemiology. 2011;30(2):194-6.	Excluded by title
108	He MX, Zhang CN. Investigation of children's intelligence quotient and dental fluorosis in drinking water-type of endemic fluorosis area in Pucheng county Shaanxi province before and after drinking water change. Chinese Journal of Endemiology. 2010;29(5):547-8.	Excluded by title
109	Hebbal M, Nagarajappa R. Does school-based dental screening for children increase follow-up treatment at dental school clinics? Journal of dental education. 2005;69(3):382-6.	Excluded by title

110	Hennon D, Stookey G, Beiswanger B. Fluoride-vitamin supplements: effects on dental caries and fluorosis when used in areas with suboptimum fluoride in the water supply. J Am Dent Assoc 1977; 95(5):[965-71 pp.].	Excluded by title
111	Hernandez-Guerrero JC, de la Fuente-Hernandez J, Jimenez-Farfan MD, Ledesma-Montes C, Castaneda-Castaneira E, Molina-Frechero N, et al. Fluoride content in table salt distributed in Mexico City, Mexico. Journal of public health dentistry. 2008;68(4):242-5.	Excluded by title
112	Holt R, Morris C, Winter G, Downer M. Enamel opacities and dental caries in children who used a low fluoride toothpaste between 2 and 5 years of age. International dental journal. 1994; 44(4):[331-41 pp.].	Excluded by title
113	Hou CC, Han SQ, Liu ZH, Liu HL. Investigation on the prevalent condition of adult osteofluorosis in the endemic fluorosis areas of Tianjin in 2008. Chinese Journal of Endemiology. 2010;29(3):322-4.	Excluded by title
114	Houwink B, Wagg B. Effect of fluoride dentifrice usage during infancy upon enamel mottling of the permanent teeth. Caries research. 1979; 13(4).	Excluded by title
115	Huang CQ, Wang CH, Zhang XL, Wu SJ, Lu ZM, Liang BC, et al. Clinical manifestation and significance of dental fluorosis of children in endemic fluorosis areas and non-diseases areas. Chinese Journal of Endemiology. 2005;24(1):64-6.	Excluded by title
116	Hujoel P, Zina L, Moimaz S, Cunha-Cruz J. Infant formula and enamel fluorosis: a systematic review (Structured abstract). Journal of the American Dental Association. 2009; 140(7):[841-54 pp.].	Excluded by title
117	Hujoel PP, Zina LG, Moimaz SA, Cunha-Cruz J. Infant formula and enamel fluorosis: a systematic review. J Am Dent Assoc 2009;140(7):841-54.	Excluded by title
118	Iheozor-Ejiofor Z, Worthington HV, Walsh T, O'Malley L, Clarkson JE, Macey R, et al. Water fluoridation for the prevention of dental caries. Cochrane Database of Systematic Reviews. 2015; (6).	Excluded by title
119	Isci D, Sahin Saglam AM, Alkis H, Elekdag-Turk S, Turk T. Effects of fluorosis on the shear bond strength of orthodontic brackets bonded with a self-etching primer. European journal of orthodontics. 2011;33(2):161-6.	Excluded by title
120	Ismail A, Hasson H. Fluoride supplements, dental caries and fluorosis: a systematic review (Structured abstract). Journal of the American Dental Association. 2008; 139(11):[1457-68 pp.].	Excluded by title
121	Ismail AI, Bandekar RR. Fluoride supplements and fluorosis: a meta-analysis (Structured abstract). Community dentistry and oral epidemiology. 1999; 27(1):[48-56 pp.].	Excluded by title
122	Ismail AI, Brodeur JM, Kavanagh M, Boisclair G, Tessier C, Picotte L. Prevalence of dental caries and dental fluorosis in students, 11-17 years of age, in fluoridated and non-fluoridated cities in Quebec. Caries research. 1990;24(4):290-7.	Excluded by title
123	Ismail AI, Messer JG, Hornett PJ. Prevalence of dental caries and fluorosis in seven- to 12-year-old children in northern Newfoundland and Forteau, Labrador. Journal (Canadian Dental Association). 1998;64(2):118-24.	Excluded by title
124	Jarvis HG, Heslop P, Kisima J, Gray WK, Ndossi G, Maguire A, et al. Prevalence and aetiology of juvenile skeletal fluorosis in the south-west of the Hai district, Tanzania--a community-based prevalence and case-control study. Tropical medicine & international health : TM & IH. 2013;18(2):222-9.	Excluded by title
125	Jia LH, Ma J, Du YG, Ma DR, Yao GJ, Liang SL, et al. The investigation of drinking-water-borne endemic fluorosis in Hebei province in 2009. Chinese Journal of Endemiology. 2011;30(2):184-7.	Excluded by title
126	Jiang M, Wang H, Mu L. Meta-analysis of the effectiveness of health education interventions on endemic fluorosis for Chinese students and housewives (Provisional abstract). Database of Abstracts of Reviews of Effects. 2014;2:207-10.	Excluded by title
127	Jiang Y, Foster Page LA, McMillan J, Lyons K, Broadbent J, Morgaine KC. Is New Zealand water fluoridation justified? New Zealand Medical Journal. 2014;127(1406):80-6.	Excluded by title
128	Johansson AK, Johansson A, Birkhed D, Omar R, Baghdadi S, Carlsson GE. Dental erosion, soft-drink intake, and oral health in young Saudi men, and the development of a system for assessing erosive anterior tooth wear. Acta odontologica Scandinavica. 1996;54(6):369-78.	Excluded by title
129	Johansson AK, Johansson A, Birkhed D, Omar R, Baghdadi S, Khan N, et al. Dental erosion associated with soft-drink consumption in young Saudi men. Acta odontologica Scandinavica. 1997;55(6):390-7.	Excluded by title
130	Julien KC, Buschang PH, Campbell PM. Prevalence of white spot lesion formation during orthodontic treatment. The Angle orthodontist. 2013;83(4):641-7.	Excluded by title
131	Kadir RA, Al-Maqtari RA. Endemic fluorosis among 14-year-old Yemeni adolescents: an exploratory survey. International dental journal. 2010;60(6):407-10.	Excluded by title
132	Kanagaratnam S, Schluter P, Durward C, Mahood R, Mackay T. Enamel defects and dental caries in 9-year-old children living in fluoridated and nonfluoridated areas of Auckland, New Zealand. Community dentistry and oral epidemiology. 2009;37(3):250-9.	Excluded by title
133	Khan SA, Singh RK, Navit S, Chadha D, Johri N, Navit P, et al. Relationship between dental fluorosis and intelligence quotient of school going children in and around lucknow district: A cross-sectional study. Journal of Clinical and Diagnostic Research. 2015;9(11):ZC10-ZC5.	Excluded by title
134	Khandare A, Rasaputra K, Meshram I, Rao S. Effects of smoking, use of aluminium utensils, and tamarind consumption on fluorosis in a fluorotic village of Andhra Pradesh, India. Fluoride. 2010;43(2):128-33.	Excluded by title
135	Khandare AL, Rao GS, Lakshmaiah N. Effect of tamarind ingestion on fluoride excretion in humans. European Journal of Clinical Nutrition. 2002;56(1):82-5.	Excluded by title
136	Kirkegaard E, Larsen M, Poulsen S, Fejerskov O. Dental fluorosis among participants in a non-supervised fluoride tablet program [abstract]. Journal of dental research. 1988; 67(4):[769, Abstract no: 151 pp.].	Excluded by title
137	Kirzioğlu Z, Ertürk MSÖ, Karayilmaz H. Evaluation of dental caries and nursing caries prevalence in pre-school children living in a high fluoride area of Turkey. Fluoride. 2004;37(4):278-90.	Excluded by title
138	Kobayashi CAN, Belini MR, Italiani FDM, Pauleto ARC, Julianelli De Araújo J, Tessarolli V, et al. Factors influencing fluoride ingestion from dentifrice by children. Community dentistry and oral epidemiology. 2011;39(5):426-32.	Excluded by title
139	Kong HY, Zhou W, Guo PH, Sang ZC, Wu GN, Chen YJ, et al. Safety of individual medication of Ma Qian Zi (semen strychni) based upon assessment of therapeutic effects of Guo's therapy against moderate fluorosis of bone. Journal of traditional Chinese medicine = Chung i tsa chih ying wen pan. 2011;31(4):297-302.	Excluded by title
140	Kravchenko J, Rango T, Akushevich I, Atlaw B, McCornick PG, Merola RB, et al. The effect of non-fluoride factors on risk of dental fluorosis: evidence from rural populations of the Main Ethiopian Rift. The Science of the total environment. 2014;488-489:595-606.	Excluded by title
141	Kukleva MP, Isheva AV, Kondeva VK, Dimitrova MM, Petrova SG. Prevalence of dental fluorosis among 4- to 14-year-old children from the town of Dimitrovgrad (Bulgaria). Folia medica. 2007;49(1-2):25-31.	Excluded by title
142	Kumar S, Kroon J, Lalloo R, Johnson NW. Validity and reliability of short forms of parental-caregiver perception and family impact scale in a Telugu speaking population of India. Health and quality of life outcomes. 2016;14:34.	Excluded by title
143	Lacerenza S, Stronati M, Paolillo P, Romagnoli C. Vitamin D and fluoride: In order to prevent, not to cure. Early Human Development. 2013;89(SUPPL4):S121-S2.	Excluded by title

144	Lalumandier JA, Rozier RG. The prevalence and risk factors of fluorosis among patients in a pediatric dental practice. Pediatric dentistry. 1995;17(1):19-25.	Excluded by title
145	Lawson J, Warren JJ, Levy SM, Broffitt B, Bishara SE. Relative esthetic importance of orthodontic and color abnormalities. The Angle orthodontist. 2008;78(5):889-94.	Excluded by title
146	Leroux BG, Maynard RJ, Domoto P, Zhu C, Milgrom P. The estimation of caries prevalence in small areas. Journal of dental research. 1996;75(12):1947-56.	Excluded by title
147	Leverett DH, Adair SM, Vaughan BW, Proskin HM, Moss ME. Randomized clinical trial of the effect of prenatal fluoride supplements in preventing dental caries. Caries research. 1997;31(3):174-9.	Excluded by title
148	Levine RS, Beal JF, Fleming CM. A photographically recorded assessment of enamel hypoplasia in fluoridated and non-fluoridated areas in England. British dental journal. 1989;166(7):249-52.	Excluded by title
149	Li DS, An D, He P, Liang Y, Jin ZJ. Influence of stove and coal-burning mode on formation of severe endemic fluorosis regions in Guizhou Province. Chinese Journal of Endemiology. 2008;27(2):183-7.	Excluded by title
150	Li Y, Jing X, Chen D, Lin L, Wang Z. Effects of endemic fluoride poisoning on the intellectual development of children in baotou. Fluoride. 2008;41(2):161-4.	Excluded by title
151	Liu HL, Fang J, Feng LH, Xu YJ, Ding XC, Zheng HH, et al. Effect of dietary nutrition on dental fluorosis degrees in school children. Chinese Journal of Endemiology. 2009;28(3):325-8.	Excluded by title
152	Liu J, Xia T, Zhang M, He W, He P, Chen X, et al. Screening of environmental response genes related to dental fluorosis. Fluoride. 2006;39(3):195-201.	Excluded by title
153	Liu M, Qian C. [Effect of endemic fluorosis on children's intelligence development: a Meta analysis]. Zhongguo dang dai er ke za zhi = Chinese journal of contemporary pediatrics. 2008;10(6):723-5.	Excluded by title
154	Liu XQ, Li ZM, Ma CB, Zhang D, Sun ZH. Shear bond strength of recycled metal brackets. Journal of Clinical Rehabilitative Tissue Engineering Research. 2008;12(1):193-5.	Excluded by title
155	Locker D. Disparities in oral health-related quality of life in a population of Canadian children. Community dentistry and oral epidemiology. 2007;35(5):348-56.	Excluded by title
156	Loyola-Rodríguez JP, De Jesús Pozos-Guillén A, Hernández-Guerrero JC, Hernández-Sierra JF. Dental fluorosis in primary dentition in an endemic hydrofluorosis area. Salud publica de Mexico. 2000;42(3):194-200.	Excluded by title
157	Loyola-Rodriguez JP, Pozos-Guillen AJ, Hernandez-Guerrero JC, Hernandez-Sierra JF. [Fluorosis in primary dentition in a region with endemic water fluoride]. Salud publica de Mexico. 2000;42(3):194-200.	Excluded by title
158	Macpherson LM, Conway DI, Gilmour WH, Petersson LG, Stephen KW. Photographic assessment of fluorosis in children from naturally fluoridated Kungsbacka and non-fluoridated Halmstad, Sweden. Acta odontologica Scandinavica. 2007;65(3):149-55.	Excluded by title
159	Maguire A, Zohouri FV, Hindmarch PN, Hatts J, Moynihan PJ. Fluoride intake and urinary excretion in 6-to 7-year-old children living in optimally, sub-optimally and non-fluoridated areas. Community dentistry and oral epidemiology. 2007;35(6):479-88.	Excluded by title
160	Mahesh Kumar P, Joseph T, Varma RB, Jayanthi M. Oral health status of 5 years and 12 years school going children in Chennai city--an epidemiological study. Journal of the Indian Society of Pedodontics and Preventive Dentistry. 2005;23(1):17-22.	Excluded by title
161	Mapengo MA, Marsicano JA, Garcia de Moura P, Sales-Peres A, Hobdell M, de Carvalho Sales-Peres SH. Dental caries in adolescents from public schools in Maputo, Mozambique. International dental journal. 2010;60(4):273-81.	Excluded by title
162	Mapengo MAA. Condições de saúde bucal em adolescentes de Maputo, Moçambique. 2010:122-.	Excluded by title
163	Marinho VC, Higgins JP, Sheiham A, Logan S. Fluoride toothpastes for preventing dental caries in children and adolescents. The Cochrane database of systematic reviews. 2003(1):Cd002278.	Excluded by title
164	Martinez-Mier EA, Kelly SA, Eckert GJ, Jackson RD. Comparison of a dietary survey and the duplicate plate method for determining dietary fluoride ingested by young children: a pilot study. International journal of paediatric dentistry. 2009;19(2):99-107.	Excluded by title
165	Martinez-Mier EA, Soto-Rojas AE, Buckley CM, Zero DT, Margineda J. Fluoride concentration of bottled water, tap water, and fluoridated salt from two communities in Mexico. International dental journal. 2005;55(2):93-9.	Excluded by title
166	Meneghim MdC, Esmeriz CEdC, Vilas-Boas P, Meneghim ZMP, Pereira AAC. Impacto de programas educativos sobre condições bucais de escolares de 6 e 7 anos em duas escolas municipais do interior do Estado de São Paulo/Brasil. Arq Cent Estud Curso Odontol Univ Fed Minas Gerais. 2012;48(01):40-6.	Excluded by title
167	Mestriner SF, Morrayne MA, Aguila AP, Ferraudo AS, Mestriner Júnior W. Fatores associados à cárie dentária em escolares aos 12 anos em um município do estado de São Paulo, Brasil. RGO. 2013;61(1):69-75.	Excluded by title
168	México. Secretaria de Salud. Subjefatura de Regulación S. Informe epidemiológico del estudio integral de la contaminación en el Valle del Guadiana, Durango. 1989:41-.	Excluded by title
169	Moraes SM, Pessan JP, Ramires I, Buzalaf MA. Fluoride intake from regular and low fluoride dentifrices by 2-3-year-old children: influence of the dentifrice flavor. Brazilian oral research. 2007;21(3):234-40.	Excluded by title
170	Moura MSd, Gomes LdMA, Castro MRPd, Teles JBM, Moura LdFAdD. Fluorose dentária em escolares de 12 anos. RGO. 2010;58(4):463-8.	Excluded by title
171	Moysés SJ, Moysés ST, Allegretti ACV, Argenta M, Werneck R. Fluorose dental: ficção epidemiológica? Rev Panam Salud Publica. 2002;12(5):339-46.	Excluded by title
172	Muwazi LM, Rwenyonyi CM, Tirwomwe FJ, Ssali C, Kasangaki A, Nkamba ME, et al. Prevalence of oral diseases/conditions in Uganda. African health sciences. 2005;5(3):227-33.	Excluded by title
173	Nagpal DI, Damle SG. Comparison of salivary fluoride levels following use of dentifrices containing different concentrations of fluoride. Journal of the Indian Society of Pedodontics and Preventive Dentistry. 2007;25(1):20-2.	Excluded by title
174	Negri H, Cury J. [Dose-response effect of a dentifrice formulation with low fluoride concentration - an in vitro study]. Pesquisa odontologica brasileira = Brazilian oral research. 2002; 16(4):[361-5 pp.].	Excluded by title
175	Nirgude AS, Saiprasad GS, Naik PR, Mohanty S. An epidemiological study on fluorosis in an urban slum area of Nalgonda, Andhra Pradesh, India. Indian journal of public health. 2010;54(4):194-6.	Excluded by title
176	Niu ZH, Zhao JL. Analysis of monitoring data of drinking-water borne endemic fluorosis in Xinzhou of Shanxi province in 2010. Chinese Journal of Endemiology. 2012;31(3):321-4.	Excluded by title
177	Nowjack-Raymer RE, Selwitz RH, Kingman A, Driscoll WS. The prevalence of dental fluorosis in a school-based program of fluoride mouthrinsing, fluoride tablets, and both procedures combined. Journal of public health dentistry. 1995;55(3):165-70.	Excluded by title
178	Nowjack-Raymer RE, Selwitz RH, Kingman A, Driscoll WS. The Prevalence of Dental Fluorosis in a School-based Program of Fluoride Mouthrinsing, Fluoride Tablets, and Both Procedures Combined. Journal of public health dentistry. 1995;55(3):165-70.	Excluded by title
179	Nunn JH, Murray JJ, Reynolds P, Tabari D, Breckon J. The prevalence of developmental defects of enamel in 15-16-year-old children residing in three districts (natural fluoride, adjusted fluoride, low fluoride) in the north east of England. Community dental health. 1992;9(3):235-47.	Excluded by title

180	Olivares-Keller D, Arellano-Valeria MJ, Cortés J, Cantín M. Prevalencia y severidad de fluorosis dental y su asociación con historia de caries en escolares que consumen agua potable fluorurada en temuco, Chile. Int j odontostomatol (Print). 2013;7(3):447-54.	Excluded by title
181	Oliveira BH, Milbourne P. [Dental fluorosis in upper permanent incisors of public schoolchildren in Rio de Janeiro, Brazil]. Revista de saude publica. 2001;35(3):276-82.	Excluded by title
182	Oliveira LFBd, Souza JGS, Mendes RIP, Oliveira RCN, Oliveira CdC, Lima CV, et al. A presença de fluorose dentária estaria associada ao traumatismo dentário entre escolares? Ciênc saúde coletiva. 2016;21(3):967-76.	Excluded by title
183	Oliveira MJ, Paiva SM, Martins LH, Ramos-Jorge ML, Lima YB, Cury JA. Fluoride intake by children at risk for the development of dental fluorosis: comparison of regular dentifrices and flavoured dentifrices for children. Caries research. 2007;41(6):460-6.	Excluded by title
184	Organización Panamericana de la S, México. Secretaría de S. Informe conjunto de trabajo de salud oral. 1998:[50]-[].	Excluded by title
185	Pan S, An W, Li H, Yang M. [Using fractional polynomials to estimate the safety threshold of fluoride in drinking water]. Wei sheng yan jiu = Journal of hygiene research. 2014;43(1):27-31.	Excluded by title
186	Pendrys DG, Haugejorden O, Bardsen A, Wang NJ, Gustavsen F. The risk of enamel fluorosis and caries among Norwegian children: implications for Norway and the United States. J Am Dent Assoc 2010;141(4):401-14.	Excluded by title
187	Pereira AC, Da Cunha FL, Meneghim Mde C, Werner CW. Dental caries and fluorosis prevalence study in a nonfluoridated Brazilian community: trend analysis and toothpaste association. ASDC journal of dentistry for children. 2000;67(2):132-5, 83.	Excluded by title
188	Pretty IA. High Fluoride Concentration Toothpastes for Children and Adolescents. Caries research. 2016;50:9-14.	Excluded by title
189	Ramezani GH, Valaei N, Eikani H. Prevalence of DMFT and fluorosis in the students of Dayer city (Iran). Journal of the Indian Society of Pedodontics and Preventive Dentistry. 2004;22(2):49-53.	Excluded by title
190	Ramires I, Grec RH, Cattan L, Moura PG, Lauris JR, Buzalaf MA. [Evaluation of the fluoride concentration and consumption of mineral water]. Revista de saude publica. 2004;38(3):459-65.	Excluded by title
191	Ramírez Puerta BS, Franco Cortés ÁM, Gómez Restrepo ÁM, Corrales Mesa DI. Fluorosis dental en escolares de instituciones educativas privadas. Medellín, Colombia, 2007. Rev Fac Odontol Univ Antioq. 2010;21(2):170-6.	Excluded by title
192	Ranga A, Sharma J, Rathore H, Mathur G. Sodium fluoride induced toxicity in testes of Swiss albino mice and it's reversal by ascorbic acid and calcium. International Journal of Pharmaceutical Sciences Review and Research. 2014;24(2):99-104.	Excluded by title
193	Rihs LB, Silva RC, Sousa MdLRd, Cypriano S, Gomes PR. Atividade de cárie em adolescentes de município com muito baixa prevalência de cárie: Paulínia, São Paulo, 2004. Rev Fac Odontol P Alegre. 2007;48(1/3):12-6.	Excluded by title
194	Rihs LB, Sousa MdLRd, Cypriano S, Abdalla NM, Guidini DDN, Amgarten C. Atividade de cárie na dentição decídua, Indaiatuba, São Paulo, Brasil, 2004. Cadernos de saude publica. 2007;23(3):593-600.	Excluded by title
195	Riordan PJ. Dental-Caries and Fluoride Exposure in Western Australia. Journal of dental research. 1991;70(7):1029-34.	Excluded by title
196	Roncalli AG, Silva NNd, Nascimento AC, Freitas CHSdM, Casotti E, Peres KG, et al. Aspectos metodológicos do Projeto SBBrasil 2010 de interesse para inquéritos nacionais de saúde. Cadernos de saude publica. 2012;28(supl):s40-s57.	Excluded by title
197	Rwenyonyi C, Bjorvatn K, Birkeland J, Haugejorden O. Altitude as a risk indicator of dental fluorosis in children residing in areas with 0.5 and 2.5 mg fluoride per litre in drinking water. Caries research. 1999;33(4):267-74.	Excluded by title
198	Sabieha AM, Rock WP. A comparison of clinical and photographic scoring using the TF and modified DDE indices. Community dental health. 1998;15(2):82-7.	Excluded by title
199	Sagheri D, McLoughlin J, Clarkson JJ. The prevalence of dental fluorosis in relation to water or salt fluoridation and reported use of fluoride toothpaste in school-age children. Eur Arch Paediatr Dent 2007;8(1):62-8.	Excluded by title
200	Sami E, Vichayanrat T, Satitvipawee P. Caries with Dental fluorosis and oral health behaviour among 12-year school children in moderate-fluoride drinking water community in Quetta, Pakistan. Journal of the College of Physicians and Surgeons Pakistan. 2016;26(9):744-7.	Excluded by title
201	Santos A, Oliveira B, Nadanovsky P. Effects of low and standard fluoride toothpastes on caries and fluorosis: systematic review and meta-analysis (Provisional abstract). Caries research. 2013; 47(5):[382-90 pp.].	Excluded by title
202	Santos AP, Oliveira BH, Nadanovsky P. Effects of low and standard fluoride toothpastes on caries and fluorosis: systematic review and meta-analysis. Caries research. 2013;47(5):382-90.	Excluded by title
203	Santos APPd. Efeito do dentifrício fluoretado na incidência de cárie na dentição decídua e fluorose na dentição permanente: revisões sistemáticas e metanálises. 2011:156-.	Excluded by title
204	Senewiratne B, Senewiratne K, Hettiarachchi J, Thambipillai S. Assessment of the fluoride content of water in wells selected randomly and after examining schoolchildren for dental fluorosis. Bulletin of the World Health Organization. 1973;49(4):419-22.	Excluded by title
205	Shanbhog R, Nikitha BS, Nandlal B, Thippeswamy M. Effect of dentifrice of varying fluoride concentration on surface microhardness of fluorosed enamel: an in vitro study. European Archives of Paediatric Dentistry. 2016;17(4):257-64.	Excluded by title
206	Shekar C, Cheluvaiah MB, Namile D. Prevalence of dental caries and dental fluorosis among 12 and 15 years old school children in relation to fluoride concentration in drinking water in an endemic fluoride belt of Andhra Pradesh. Indian journal of public health. 2012;56(2):122-8.	Excluded by title
207	Shi RX, Zhu XC, Chen YP, Zhou YM. Effects of different etching methods on losing ratio of bond orthodontic brackets in fluorotic teeth. Journal of Jilin University Medicine Edition. 2011;37(2):319-22.	Excluded by title
208	Shu CL, Wang CS, Wang Y, Xia YT, Chen SH. Analysis of surveillance results of drinking-water-borne endemic fluorosis in Jiangsu Province in 2009. Chinese Journal of Endemiology. 2013;32(6):662-7.	Excluded by title
209	Shulman JD, Lalumandier JA, Grabenstein JD. The average daily dose of fluoride: a model based on fluid consumption. Pediatric dentistry. 1995;17(1):13-8.	Excluded by title
210	Siew Tan B, Razak IA. Fluoride exposure from ingested toothpaste in 4-5-year-old Malaysian children. Community dentistry and oral epidemiology. 2005;33(5):317-25.	Excluded by title
211	Silva APd, Rosa DPd, Castilhos EDd, Bighetti TI. Prevalência de fluorose dentária nos municípios de Sobradinho e Tavares, Rio Grande do Sul, 2010. Rev Fac Odontol P Alegre. 2010;51(2):19-24.	Excluded by title
212	Silva SRCd, Fernandes CE, Alves RX. Condição da saúde bucal de escolares e pré-escolares, Araraquara - SP, 2004. Rev Odontol UNESP. 2007;36(2):145-50.	Excluded by title
213	Singh A, Purohit B, Sequeira P, Acharya S. Oral health status of 5-year-old Aborigine children compared with similar aged marginalised group in south western India. International dental journal. 2011;61(3):157-62.	Excluded by title
214	Singh A, Sequiera P, Acharya S, Bhat M. Oral health status of two 12-year-old socially disadvantaged groups in South India: a comparative study. Oral health & preventive dentistry. 2011;9(1):3-7.	Excluded by title
215	Sjogren K, Ekstrand J, Birkhed D. Effect of Water Rinsing after Toothbrushing on Fluoride Ingestion and Absorption. Caries research. 1994;28(6):455-9.	Excluded by title
216	Somani A, Newton JT, Dunne S, Gilbert DB. The impact of visible dental decay on social judgements: comparison of the effects of location and extent of lesion. International dental journal. 2010;60(3):169-74.	Excluded by title

217	Song GH, Gao JP, Wang CF, Chen CY, Yan XY, Guo M, et al. Sodium fluoride induces apoptosis in the kidney of rats through caspase-mediated pathways and DNA damage. Journal of physiology and biochemistry. 2014;70(3):857-68.	Excluded by title
218	Soto-Rojas AE, Martinez-Mier EA, Urena-Cirett J, Jackson RD, Stookey GK. Development of a standardisation device for photographic assessment of dental fluorosis in field studies. Oral health & preventive dentistry. 2008;6(1):29-36.	Excluded by title
219	Spohr AR, Menegaz AM, Favetti M, Flores RZ, Horn T, Benetti T, et al. Prevalência de fluorose dentária em adolescentes de escolas municipais da área urbana do município de Pelotas/RS, 2010. Rev Fac Odontol P Alegre. 2010;51(3):5-10.	Excluded by title
220	Steiner M, Helfenstein U, Menghini G. Effect of 1000 ppm relative to 250 ppm fluoride toothpaste. A meta-analysis. American journal of dentistry. 2004;17(2):85-8.	Excluded by title
221	Steiner M, Menghini G, Thomet E, Jager A, Pfister J, Imfeld T. Assessment of dental fluorosis prevalence in Swiss populations. Schweizer Monatsschrift fur Zahnmedizin = Revue mensuelle suisse d'odonto-stomatologie = Rivista mensile svizzera di odontologia e stomatologia. 2010;120(1):12-20.	Excluded by title
222	Stephen KW, Macpherson LM, Gorzo I, Gilmour WH. [Caries, fluorosis and salt fluoridation in the city of Szeged]. Fogorvosi szemle. 1998;91(8-9):275-80.	Excluded by title
223	Stephen KW. Use of fluoride. Lancet (London, England). 1999;354(9172):74-5.	Excluded by title
224	Subramaniam P, Babu KL, Naveen HK. Effect of tooth preparation on sealant success--an in vitro study. J Clin Pediatr Dent 2009;33(4):325-31.	Excluded by title
225	Subramaniam P, Kl GB, Hk N. Effect of tooth preparation on sealant success-an in vitro study. Journal of Clinical Pediatric Dentistry. 2009;33(4):325-31.	Excluded by title
226	Sukhabogi JR, Parthasarathi P, Anjum S, Chandra Shekar BR. Prevalence of dental caries and dental fluorosis among 12 and15 year-old school children in an endemic fluoride area of Nalgonda district, Andhra Pradesh, India. Annals of Tropical Medicine and Public Health. 2013;6(4):422-9.	Excluded by title
227	Sumida DH, Chiba FY, Colombo NH, Shirakashi DJ, Garbin CAS. The chronic exposure to fluoride inhibits insulin signal in the adipose tissue and causes insulin resistance in rats. Diabetes. 2011;60:A677.	Excluded by title
228	Sun D, Gao Y, Zhao L, Wang C, Wang W, Gao L. Analysis on the monitoring results of drinking water borne endemic fluorosis in China (2009-2011). Fluoride. 2012;45(3):204-5.	Excluded by title
229	Taheri Tanjani P, Moradinazar M, Esmail Mottlagh M, Najafi F. The prevalence of diabetes mellitus (DM) type II among Iranian elderly population and its association with other age-related diseases, 2012. Archives of Gerontology and Geriatrics. 2015;60(3):373-9.	Excluded by title
230	Tan BS, Razak IA, Foo LC. Fluorosis prevalence among schoolchildren in a fluoridated community in Malaysia. Community dental health. 2005;22(1):35-9.	Excluded by title
231	Tapsoba H, Bakayoko-Ly R. Oral health status of 12-year-old schoolchildren in the province of Kadiogo, Burkina Faso. Community dental health. 2000;17(1):38-40.	Excluded by title
232	Tavener JA, Davies GM, Davies RM, Ellwood RP. The prevalence and severity of fluorosis and other developmental defects of enamel in children who received free fluoride toothpaste containing either 440 or 1450 ppm F from the age of 12 months. Community dental health. 2004;21(3):217-23.	Excluded by title
233	Tavener JA, Davies GM, Davies RM, Ellwood RP. The prevalence and severity of fluorosis in children who received toothpaste containing either 440 or 1,450 ppm F from the age of 12 months in deprived and less deprived communities. Caries research. 2005;40(1):66-72.	Excluded by title
234	Tavener JA, Davies GM, Davies RM, Ellwood RP. The prevalence and severity of fluorosis in children who received toothpaste containing either 440 or 1,450 ppm F from the age of 12 months in deprived and less deprived communities. Caries research. 2006;40(1):66-72.	Excluded by title
235	Tay HL, Zainudin IS, Jaafar N. Fluoride toothpaste utilization behaviour among preschool children in Perlis, Malaysia. Community dental health. 2009;26(4):211-5.	Excluded by title
236	Tubert-Jeannin S, Auclair C, Amsallem E, Tramini P, Gerbaud L, Ruffieux C, et al. Fluoride supplements (tablets, drops, lozenges or chewing gums) for preventing dental caries in children. The Cochrane database of systematic reviews. 2011(12):Cd007592.	Excluded by title
237	Universidad Mayor. Facultad de O. Diagnóstico nacional de salud bucal del adolescente de 12 años y evaluación del grado de cumplimiento de los objetivos sanitarios de salud bucal 2000-2010. Documentos Técnicos. 2007:131-.	Excluded by title
238	Uribe S. Prevention and management of dental decay in the pre-school child. Evidence-Based Dentistry. 2006;7(1):4-7.	Excluded by title
239	Vilasrao GS, Kamble KM, Sabat RN. Child fluorosis in Chhattisgarh, India: a community-based survey. Indian pediatrics. 2014;51(11):903-5.	Excluded by title
240	Vilhena FV, Olympio KP, Lauris JR, Delbem AC, Buzalaf MA. Low-fluoride acidic dentifrice: a randomized clinical trial in a fluoridated area. Caries research. 2010;44(5):478-84.	Excluded by title
241	Vilhena FV. Eficácia de um novo dentifrício líquido com baixa concentração de flúor e pH acidulado na prevenção de lesões cariosas: estudo clínico randomizado. 2008:129-.	Excluded by title
242	Waidyasekera K, Nikaido T, Weerasinghe D, Watanabe A, Ichinose S, Tay F, et al. Why does fluorosed dentine show a higher susceptibility for caries: an ultra-morphological explanation. Journal of medical and dental sciences. 2010;57(1):17-23.	Excluded by title
243	Walker M, Rondeau M, Petrie C, Tasca A, Williams K. Surface quality and long-term dimensional stability of current elastomeric impression materials after disinfection. Journal of prosthodontics : official journal of the American College of Prosthodontists. 2007; 16(5):[343-51 pp.].	Excluded by title
244	Walsh T, Worthington HV, Glenny AM, Appelbe P, Marinho VC, Shi X. Fluoride toothpastes of different concentrations for preventing dental caries in children and adolescents. The Cochrane database of systematic reviews. 2010(1):Cd007868.	Excluded by title
245	Wang C, Gao Y, Wang W, Zhao L, Zhang W, Han H, et al. A national cross-sectional study on effects of fluoride-safe water supply on the prevalence of fluorosis in China. BMJ Open. 2012;2(5).	Excluded by title
246	Wang C, Zhang W, Zhao LJ, Gao YH. National monitoring report of drinking-water-borne endemic fluorosis in 2010. Chinese Journal of Endemiology. 2012;31(4):412-8.	Excluded by title
247	Wang JY, Li BL, Zhao XH, Huang YX, Chen JK, Chen SH, et al. Effects of drinking water defluoride in endemic fluorosis areas in Shantou city of Guangdong province. Chinese Journal of Endemiology. 2013;32(1):71-3.	Excluded by title
248	Wang S, Zhang H, Fan W, Fang S, Kang P, Chen X, et al. The effects of endemic fluoride poisoning caused by coal burning on the physical development and intelligence of children. Fluoride. 2008;41(4):344-8.	Excluded by title
249	Wang Y, Chen XD, Wang CS. Using inverse distance weighting in studying the distribution of endemic fluorosis in Jiangsu Province. Chinese Journal of Endemiology. 2009;28(1):97-100.	Excluded by title
250	Weeks KJ. Desmond Greer Walker Award. Enamel mottling in a non-fluoride community since the advent of fluoride toothpastes. British dental journal. 1990;169(8):258-60.	Excluded by title
251	Wei S, Kanellis M. Fluoride retention after sodium fluoride mouthrinsing by preschool children. J Am Dent Assoc 1983; 106(5).	Excluded by title

252	Wei S, Lu Q, Yang P, Li S, Jiang H, Chen P, et al. Epidemic status of drinking-tea-borne fluorosis in different occupational groups in Qinghai Province. Chinese Journal of Endemiology. 2014;33(2):164-6.	Excluded by title
253	Wei SY, He DL, Ding P, Pu GL, Lu Q, Yang P, et al. Analysis of surveillance results of drinking water type of endemic fluorosis in Qinghai province in 2009. Chinese Journal of Endemiology. 2011;30(5):542-5.	Excluded by title
254	Wei SY, Lu Q, Ding P, Ding SR, Pu GL, Chen P, et al. Outcome analysis on drinking-water type endemic fluorosis in Qinghai in 2008. Chinese Journal of Endemiology. 2010;29(1):77-9.	Excluded by title
255	Whelton H, Crowley E, O'Mullane D, Donaldson M, Cronin M, Kelleher V. Dental caries and enamel fluorosis among the fluoridated population in the Republic of Ireland and non fluoridated population in Northern Ireland in 2002. Community dental health. 2006;23(1):37-43.	Excluded by title
256	Whelton H, Crowley E, O'Mullane D, Donaldson M, Kelleher V, Cronin M. Dental caries and enamel fluorosis among the fluoridated and non-fluoridated populations in the Republic of Ireland in 2002. Community dental health. 2004;21(1):37-44.	Excluded by title
257	Woltgens JH, Etty EJ, Nieuwland WM, Lyaruu DM. Use of fluoride by young children and prevalence of mottled enamel. Advances in dental research. 1989;3(2):177-82.	Excluded by title
258	Wong HM, McGrath C, King NM. Diffuse opacities in 12-year-old Hong Kong children--four cross-sectional surveys. Community dentistry and oral epidemiology. 2014;42(1):61-9.	Excluded by title
259	Wong HM, McGrath C, Lo ECM, King NM. Association between developmental defects of enamel and different concentrations of fluoride in the public water supply. Caries research. 2006;40(6):481-6.	Excluded by title
260	Wong MC, Clarkson J, Glenny AM, Lo EC, Marinho VC, Tsang BW, et al. Cochrane reviews on the benefits/risks of fluoride toothpastes. Journal of dental research. 2011;90(5):573-9.	Excluded by title
261	Wong MC, Glenny AM, Tsang BW, Lo EC, Worthington HV, Marinho VC. Topical fluoride as a cause of dental fluorosis in children. The Cochrane database of systematic reviews. 2010(1):Cd007693.	Excluded by title
262	Wright JT, Hanson N, Ristic H, Whall CW, Estrich CG, Zentz RR. Fluoride toothpaste efficacy and safety in children younger than 6 years A systematic review. Journal of the American Dental Association. 2014;145(2):182-9.	Excluded by title
263	Wu JQ, Dai CF, Feng GH, Wen XZ, Lin JB. Current situation of severe diseased areas of fluorosis in Guangdong province. Chinese Journal of Endemiology. 2005;24(1):59-61.	Excluded by title
264	Wu JQ, Yin DM, Dai CF, Wu HY, Feng GH, Du GX. Surveillance on water-related endemic fluorosis in Fengshun County Guangdon Province from 1991 to 2005: An outcome analysis. Chinese Journal of Endemiology. 2007;26(2):165-7.	Excluded by title
265	Xia Y, Li BL, Zhao XH, Huang YX, Chen JK, Chen SH, et al. Prevalence of dental caries in Shantou City Guangdong Province fluorosis areas after water improvement. Chinese Journal of Endemiology. 2013;32(3):309-11.	Excluded by title
266	Yan J, Zhong ZH, Wang YX, Luo XJ, Yan W, Mu LH. An investigation of dental fluorosis of children aged 8 - 12 in Wushan and Fengjie counties of Chongqing. Chinese Journal of Endemiology. 2012;31(4):423-5.	Excluded by title
267	Yan J, Zhong ZH, Wang YX, Wang L, Yong KW, Zhang MZ, et al. A survey of epidemiological factors of coal-burning-borne endemic fluorosis in northeast of Chongqing. Chinese Journal of Endemiology. 2012;31(6):653-6.	Excluded by title
268	Yang CC, Li BL, Zhao XH, Huang YX, Chen JK, Chen SH, et al. Relationship between urinary fluoride level, incidences of dental fluorosis and caries of children in fluorosis areas after change of water sources. Chinese Journal of Endemiology. 2013;32(6):673-6.	Excluded by title
269	Ye Y, Wang W, Huo LL, Liu KK, Liu Y, Sun J, et al. An investigation of the source of fluoride in the endemic fluorosis areas of Pingxiang city, Jiangxi province in 2011. Chinese Journal of Endemiology. 2013;32(1):67-70.	Excluded by title
270	Yun Z, Yin Y, Gao J, Zhang B, Bian J, Chen P. An epidemiological study of drinking water type of endemic fluorosis in Shandong Province in 2013. Chinese Journal of Endemiology. 2015;34(2):112-5.	Excluded by title
271	Yun ZJ, Chen PZ, Bian JC, Qin QL, Wang YT, Gao HX, et al. Comparative analysis on child dental fluorosis under different circumstances of water-improvement and defluoridation in Shandong Province. Chinese Journal of Endemiology. 2005;24(6):659-61.	Excluded by title
272	Yun ZJ, Chen PZ, Bian JC, Wang YT, Gao J, Ma AH, et al. Analysis of monitoring results of endemic fluorosis in Shandong province in 2009. Chinese Journal of Endemiology. 2011;30(2):188-93.	Excluded by title
273	Yusoff N, Jaafar N, Razak IA, Chew YY, Ismail N, Bulgiba AM. The prevalence of enamel opacities in permanent teeth of 11-12 year-old school children in Kuala Lumpur, Malaysia. Community dental health. 2008;25(1):55-8.	Excluded by title
274	Zaze AC, Dias AP, Amaral JG, Miyasaki ML, Sassaki KT, Delbem AC. In situ evaluation of low-fluoride toothpastes associated to calcium glycerophosphate on enamel remineralization. J Dent 2014;42(12):1621-5.	Excluded by title
275	Zhai Y, Deng F, Huang G, Gao J, Li D, Zhang S, et al. An analysis of the monitoring results of coal-burning-borne endemic fluorosis in Pu'an County in 2011-2013. Chinese Journal of Endemiology. 2015;34(8):603-5.	Excluded by title
276	Zhang B, Li D, Zhang N, He P, Hu X, Wang X. A epidemiological study of children's dental fluorosis in coal-burning-borne endemic fluorosis areas of three counties in Guizhou Province. Chinese Journal of Endemiology. 2014;33(2):167-9.	Excluded by title
277	Zhang X, Zhang K, Xu F. The effects of fluoride on testicular cell cycle and cell apoptosis of male rats. Chinese Journal of Endemiology. 2014;33(3):272-4.	Excluded by title
278	Zhao LJ, Wang C, Gao YH, Sun DJ. National annual monitoring report of drinking-water-borne endemic fluorosis in 2010 and 2011. Chinese Journal of Endemiology. 2013;32(2):177-82.	Excluded by title
279	Zina LG. Evidências científicas da associação entre fórmula infantil, fluorose e cárie dentária. 2009:235-.	Excluded by title
280	Zohoori FV, Omid N, Batterham AM, O'Hare WT, Maguire A. Comparison of estimated daily dietary fluoride intake by food diary and duplicate-plate collection methods. Proceedings of the Nutrition Society. 2012;71.	Excluded by title
281	Zuanon AC, Aranha AM. Mouthwash ingestion by preschool children. J Clin Pediatr Dent 2005;30(1):15-7.	Excluded by title
282	Arnadottir IB, Sigurjons H, Holbrook WP. Enamel opacities in 8-year-old Icelandic children in relation to their medical history as infants. Community dental health. 2005;22(4):279-81.	Excluded by abstract
283	Carrasco-Labra A, Brignardello-Petersen R, Glick M, Guyatt GH, Azarpazhooh A. A practical approach to evidence-based dentistry: VI How to use a systematic review. Journal of the American Dental Association. 2015;146(4):255-U113.	Excluded by abstract
284	Clark DC. Evaluation of aesthetics for the different classifications of the Tooth Surface Index of Fluorosis. Community dentistry and oral epidemiology. 1995;23(2):80-3.	Excluded by abstract
285	Davies GM, Pretty IA, Neville JS, Goodwin M. Investigation of the value of a photographic tool to measure self-perception of enamel opacities. BMC oral health. 2012;12:41.	Excluded by abstract
286	Duan JH, Song JY. Comparison of Shear bond strength and adhesive remnant index among three orthodontic adhesives. Journal of Clinical Rehabilitative Tissue Engineering Research. 2008;12(19):3671-3.	Excluded by abstract
287	Ertugrul F, Turkun M, Turkun LS, Toman M, Cal E. Bond strength of different dentin bonding systems to fluorotic enamel. The journal of adhesive dentistry. 2009;11(4):299-303.	Excluded by abstract

288	Ertürk MSO, Karayilmaz H, Orhan H, Kirzioğlu Z. Effects of dental fluorosis and salivary contamination on microleakage of four different restorative materials in primary molars. Fluoride. 2006;39(3):220-7.	Excluded by abstract
289	Gleber-Netto FO, Diniz IM, Mudado FA, Fraga MG, Vargas AM. Assessment of aesthetic perception of mild and moderate dental fluorosis levels among students from the Federal University of Minas Gerais-UFMG, Brazil. Oral health & preventive dentistry. 2011;9(4):339-45.	Excluded by abstract
290	Gupta A, Tangade PS, Sunil MK, Sahwney H. Investigating relationship between fluoride ION concentration in mother and cord blood serum. Medico-Legal Update. 2012;12(2):94-7.	Excluded by abstract
291	Hawley GM, Ellwood RP, Davies RM. Dental caries, fluorosis and the cosmetic implications of different TF scores in 14-year-old adolescents. Community dental health. 1996;13(4):189-92.	Excluded by abstract
292	Jia H, Zhu X-Y. Effect of three bonding adhesives on the orthodontic bracket loss rate in treating moderate and severe dental fluorosis. [Chinese]. Journal of Clinical Rehabilitative Tissue Engineering Research. 2010; 14(16):[2925-8 pp.].	Excluded by abstract
293	Jia H, Zhu XY. Effect of three bonding adhesives on the orthodontic bracket loss rate in treating moderate and severe dental fluorosis. Journal of Clinical Rehabilitative Tissue Engineering Research. 2010;14(16):2925-8.	Excluded by abstract
294	Khandare AL, Kumar PU, Shanker RG, Venkaiah K, Lakshmaiah N. Additional beneficial effect of tamarind ingestion over defluoridated water supply to adolescent boys in a fluorotic area. Nutrition (Burbank, Los Angeles County, Calif). 2004;20(5):433-6.	Excluded by abstract
295	Kukleva MP, Kondeva VK, Isheva AV, Petrova SG, Rimalovska SI. Aesthetic perception of dental fluorosis--opinions of dentists and non-specialists. Folia medica. 2010;52(2):43-8.	Excluded by abstract
296	Li A, Yan B, Tan X. [Exploration for an early discriminant model of non-skeletal phase in endemic fluorosis exposed to coal-burning]. Zhonghua yu fang yi xue za zhi [Chinese journal of preventive medicine]. 1998;32(1):16-8.	Excluded by abstract
297	Liao J, Liang X, Tian A, Zang CC, Mao L, Wang Y. Relationship of the chroma value of dental fluorosis with age and gender in the Guizhou residents. Chinese Journal of Tissue Engineering Research. 2012;16(38):7216-20.	Excluded by abstract
298	Liao J, Wang Y, Teng MH, Zhai JJ, Liang X. Chroma values of maxillary central incisors in Guizhou residents with dental fluorosis. Chinese Journal of Tissue Engineering Research. 2012;16(34):6377-81.	Excluded by abstract
299	Loyola-Rodriguez JP, Mendoza-Razo V, Rodriguez-Juarez F, Campos-Cambranis R. Flowable resin used as a sealant in molars affected by dental fluorosis: a comparative study. J Clin Pediatr Dent 2005;30(1):39-43.	Excluded by abstract
300	Martins CC, Feitosa NB, Vale MP, Paiva SM. Parents' perceptions of oral health conditions depicted in photographs of anterior permanent teeth. European journal of paediatric dentistry : official journal of European Academy of Paediatric Dentistry. 2010;11(4):203-9.	Excluded by abstract
301	Mohamed AR, Thomson WM, Mackay TD. An epidemiological comparison of Dean's index and the Developmental Defects of Enamel (DDE) index. Journal of public health dentistry. 2010;70(4):344-7.	Excluded by abstract
302	Moncada G, Sepulveda D, Elphick K, Contente M, Estay J, Bahamondes V, et al. Effects of light activation, agent concentration, and tooth thickness on dental sensitivity after bleaching. Operative dentistry. 2013;38(5):467-76.	Excluded by abstract
303	Nalweyiso N, Busingye J, Whitworth J, Robinson PG. Dental treatment needs of children in a rural subcounty of Uganda. International journal of paediatric dentistry. 2004;14(1):27-33.	Excluded by abstract
304	Noble J, Karaiskos N, Wiltshire W. In vivo bonding of orthodontic brackets to fluorosed enamel using an adhesion promotor. The Angle orthodontist. 2008; 78(2):[357-60 pp.].	Excluded by abstract
305	Si Y, Zhang BX, Hou YB, Li J, Gao XJ. [Evaluation of the psychosocial status of fluorosis patients in fluorosis epidemic areas]. Zhonghua kou qiang yi xue za zhi = Zhonghua kouqiang yixue zazhi = Chinese journal of stomatology. 2005;40(5):416-9.	Excluded by abstract
306	Stepko E. [Influence of correcting therapy course on salivary components of patients with fluorosis]. Stomatologii?a?. 2007; 86(5):[24-6 pp.].	Excluded by abstract
307	Sujak SL, Abdul Kadir R, Dom TN. Esthetic perception and psychosocial impact of developmental enamel defects among Malaysian adolescents. Journal of oral science. 2004;46(4):221-6.	Excluded by abstract
308	Vamsilatha K, Venkata KMS, Aileni KR, Sashidhar NR. Efficacy of new adhesion promoters on compromised hypocalcified enamel. Journal of Clinical and Diagnostic Research. 2015;9(7):9-11.	Excluded by abstract
309	Waidyasekera PG, Nikaido T, Weerasinghe DD, Tagami J. Bonding of acid-etch and self-etch adhesives to human fluorosed dentine. J Dent 2007;35(12):915-22.	Excluded by abstract
310	Wang QL, Chen CZ, Yao H, Zheng HS, Jiang XJ, Tian KC. Application of a method of improving the quality of sampling in review to determine the light areas of endemic fluorosis in quality control. Chinese Journal of Endemiology. 2011;30(5):572-5.	Excluded by abstract
311	Wong HM, McGrath C, King NM. Dental practitioners' views on the need to treat developmental defects of enamel. Community dentistry and oral epidemiology. 2007;35(2):130-9.	Excluded by abstract
312	Yu QH, Zhang XH, Su Y. Ultrastructural observation on the aggressiveness of self- and total-etching adhesive on enamel of dental fluorosis. Chin J Endem 2007;26(3):270-2.	Excluded by abstract
313	Zhao XG, Wu ZC, Chen ZJ, Wang JJ, Zhou JC, Pang L, et al. [Drinking-water type fluorosis treated with acupuncture of reinforcing kidney and activating spleen: a randomized controlled trial]. Zhongguo zhen jiu = Chinese acupuncture & moxibustion. 2012;32(6):485-9.	Excluded by abstract
314	Basir M, Ghomsheh E, Rezvani M, Rafie Z, Hoseini Z. [Clinical evaluation of the effect of a herbal compound made for treatment of discolorations caused by dental fluorosis]. J Dent Med 2013; 26(3):162-70.	Excluded; missing fulltext
315	Castro K, Meireles S, Ferreira A, Sampaio F, Souza C, Duarte R. Influence of two treatments for dental fluorosis in aesthetic perception [abstract]. Proceedings of the General Session of the International Association for Dental Research; 2012, Jun 20-23; Iguacu Falls, Brazil. 2012:[Abstract no: 2720 p.].	Excluded; missing fulltext
316	Coll JA, Jackson P, Strassler HE. Comparison of enamel microabrasion techniques: Prema Compound versus a 12-fluted finishing bur. J Esthet Dent 1991;3(5):180-6.	Excluded; missing fulltext
317	Haywood V, Leonard R, Nelson C, Brunson W. Effectiveness, side effects and long-term status of nightguard vital bleaching. J Am Dent Assoc. 1994 Sep;125(9):1219-26.	Excluded; missing fulltext
318	Loyola J, Pozos A, Berumen M, Hernandez F. Treatment of dental fluorosis with non Invasive techniques [abstract]. J Dent Res 2001; 80(Spec Iss).	Excluded; missing fulltext
319	Pourghadiri M, Longhurst P, Watson T. A new technique for the controlled removal of mottled enamel: measurement of enamel loss. Br Dent J 1998; 184(5):239-41.	Excluded; missing fulltext
320	Uzer CE, Yazkan B, Yildiz G. Is enamel microabrasion sufficient for aesthetic management of fluorosed teeth? [abstract]. Proceedings of the 6th General Session of the Pan European Region of the IADR; 2012, Sep 12-15; Helsinki, Finland. 2012:[Abstract no: 654 p.].	Excluded; missing fulltext
321	Wang Y, Luo N. A clinical evaluation of bleaching and enamel microabrasion for dental fluorosis [abstract]. Journal of dental research. 2002; 81(Spec Iss B [Divisional Abstracts]):[B-217, Abstract no: 11 pp.].	Excluded; missing fulltext

322	{NCT01733888} Resin Infiltration and Resin Infiltration With Bleaching in Improving the Esthetics for Fluorosis Stains. Completed	Excluded; trial registration-trial has been completed and added to references
323	{NCT02925780} Action of Infiltration Resin Icon in Fluorosis, Clinical Trial, Monitoring for 12 Month. Not yet recruiting.	Excluded; trial registration-trial still ongoing
324	Hasanuddin S, Reddy ER, Manjula M, Srilaxmi N, Rani ST, Rajesh A. Retention of fissure sealants in young permanent molars affected by dental fluorosis: a 12-month clinical study. Eur Arch Paediatr Dent 2014;15(5):309-15.	Excluded; not relevant
325	Mickenautsch S, Kopsala J, Rudolph MJ, Ogunbodede EO. Clinical evaluation of the ART approach and materials in peri-urban farm schools of the Johannesburg area. SADJ 2000;55(7):364-8.	Excluded; not relevant
326	Alkhatib MN, Holt R, Bedi R. Aesthetically objectionable fluorosis in the United Kingdom. British dental journal. 2004;197(6):325-8; discussion 1.	Excluded; no treatment
327	Do LG, Spencer A. Oral health-related quality of life of children by dental caries and fluorosis experience. Journal of public health dentistry. 2007;67(3):132-9.	Excluded; no treatment
328	Duan Y, Chen X, Wu J. Clinical comparison of bond failures using different enamel preparations of severely fluorotic teeth. J Clin Orthod 2006;40(3):152-4; quiz 9.	Excluded; no treatment
329	Welbury R. A simple technique for the removal of mottled enamel using readily available materials [comment]. Br Dent J 1998; 184(5).	Excluded; not a clinical study
330	Cocco AR, Lund RG, Torre E, Martos J. Treatment of Fluorosis Spots Using a Resin Infiltration Technique: 14-month Follow-up. Operative dentistry. 2016;41(4):357-62.	Excluded; case report/series
331	Almas K, Al-Harbi M, Al-Gunaim M. The effect of a 10% carbamide peroxide home bleaching system on the gingival health. The journal of contemporary dental practice. 2003;4(1):32-41.	Excluded; no randomization
332	Train TE, McWhorter AG, Seale NS, Wilson CF, Guo IY. Examination of esthetic improvement and surface alteration following microabrasion in fluorotic human incisors in vivo. Pediatric dentistry. 1996;18(5):353-62.	Excluded; no randomization
333	Celik E, Yildiz G, Yazkan B. Comparison of enamel microabrasion with a combined approach to the esthetic management of fluorosed teeth. Operative dentistry. 2013; 38(5):E134-e43.	Excluded; no randomization
334	Gupta S, Gupta R, Seth A, Gupta A. Reversal of fluorosis in children. Acta paediatrica Japonica; Overseas edition. 1996; 38(5):513-9.	Excluded; no randomization
335	Limeback H, Vieira AP, Lawrence H. Improving esthetically objectionable human enamel fluorosis with a simple microabrasion technique. Eur J Oral Sci 2006;114 Suppl 1:123-6.	Excluded; no randomization
336	Bharath KP, Subba Reddy VV, Poornima P, Revathy V, Kambalimath HV, Karthik B. Comparison of relative efficacy of two techniques of enamel stain removal on fluorosed teeth. An in vivo study. J Clin Pediatr Dent 2014;38(3):207-13.	Included
337	Castro KS, Ferreira AC, Duarte RM, Sampaio FC, Meireles SS. Acceptability, efficacy and safety of two treatment protocols for dental fluorosis: a randomized clinical trial. J Dent 2014;42(8):938-44.	Included
338	Gugnani N, Pandit IK, Gupta M, Gugnani S, Soni S, Goyal V. Comparative evaluation of esthetic changes in nonpitted fluorosis stains when treated with resin infiltration, in-office bleaching, and combination therapies. J Esthet Restor Dent. 2017 Jun 27. doi: 10.1111/jerd.12312. [Epub ahead of print]	Included
339	Knosel M, Attin R, Becker K, Attin T. A randomized CIE L*a*b* evaluation of external bleaching therapy effects on fluorotic enamel stains. Quintessence international (Berlin, Germany : 1985). 2008;39(5):391-9.	Included
340	Loguercio AD, Correia LD, Zago C, Tagliari D, Neumann E, Gomes OM, et al. Clinical effectiveness of two microabrasion materials for the removal of enamel fluorosis stains. Operative dentistry. 2007;32(6):531-8.	Included
341	Loyola-Rodriguez JP, Pozos-Guillen Ade J, Hernandez-Hernandez F, Berumen-Maldonado R, Patino-Marin N. Effectiveness of treatment with carbamide peroxide and hydrogen peroxide in subjects affected by dental fluorosis: a clinical trial. J Clin Pediatr Dent 2003;28(1):63-7.	Included

.

Appendix S3. Details about the risk of bias assessment of included randomized trials with the Cochrane tool.

Trial	Sequence generation	Allocation concealment	Blinding of participants/personnel	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting	Other sources of bias
Bharath 2014	Unclear – randomization description inadequate. "Each subject had one of their maxillary central incisors randomly selected for micro-abrasion and the contralateral maxillary central incisor for McInnes bleaching."	Unclear – no mention throughout the paper; Highly probable that clinician knew about the allocation, as application for the two procedures was different.	High risk – no mention of blinding of participants throughout the paper. Risk of performance bias due to probable knowledge of the allocated interventions by clinician.	Low risk (for esthetic improvement)– blinding of outcome assessment in terms of esthetic improvement is adequate: „…assessment was done by four calibrated and blinded examiners including a layperson." Examiners were checked for intra- and inter-rater reliability in advance. Unclear (for sensitivity)– In terms of sensitivity, reported by the patients, no blinding is mentioned. Outcome is patient-reported and blinding of patients has been assessed in the previous domain.	Low risk – no drop-outs or patient losses are reported. All of the patients were in follow-up for the esthetic improvement assessment. "…the pre- and post-operative photographs of 30 subjects were incorporated…" Number of patients which underwent sensitivity assessment is not mentioned, but patient loss here is highly improbable.	Unclear – no protocol exist for the trial. However, all in the trial mentioned pre-specified outcomes, such as esthetic improvement and tooth sensitivity, are reported.	Unclear – residual bias cannot be excluded.
Castro 2014	Low risk – randomization took place with a randomization table to allocate participants in each treatment group, prepared in advance by an examiner not directly involved with the clinical steps of the study.	Unclear – The randomization table for the allocation was prepared in advance "by an examiner not directly involved with the clinical steps of the study". It remains unclear if allocation was concealed and how.	High risk – no mention of blinding of participants throughout the paper. Patients and clinicians were most likely aware of the treatment, especially patients in the group with at-home bleaching had to be compliant and to know what to do.	Low risk (for esthetic improvement)– photos were assessed by two calibrated and blinded examiners. Software and digital images were used to measure stained areas objectively. Unclear (for sensitivity, satisfaction, and esthetic improvement, reported by the patients)–no blinding is mentioned. Outcome is patient-reported and blinding of patients has been assessed in the previous domain.	Low risk – no drop-outs or patient losses. All patients attended the follow-up.	Unclear – no protocol exist for the trial. However, all in the trial mentioned pre-specified outcomes, such as esthetic improvement, patient satisfaction, and tooth/gingival sensitivity, are reported.	Unclear – residual bias cannot be excluded.
Gugnani 2017	Low risk – randomization took place by using block randomization. "…children were randomly allocated in four different groups using block randomization." The random sequence generation happened web-based.	Low risk – allocation concealment was ensured by using sealed envelopes, made by an independent person a priori. "The sequence generation table was kept sealed and secured till the end of the study." "The participants were allocated to different treatment groups by independent personnel,	Unclear – either only the clinicians or only the patients are single blinded to the allocation and the treatment.	Low risk – preoperative and postoperative images were assessed by two independent observers. "To ensure blinding of the outcome evaluators, the preoperative and postoperative images were stored with a unique ID and the evaluators were not disclosed about the participant's treatment group." "Outcome evaluators were blinded to avoid any bias during the scoring of esthetic changes."	Unclear – not clearly reported.	Unclear – no protocol exist for the trial. However, all in the trial mentioned pre-specified outcomes, such as esthetic changes and improvement in opacity/stains, are reported.	Unclear – residual bias cannot be excluded.

		not involved in the sequence generation."					
Knosel 2008	Low risk – randomization took place by lot to either of the two groups.	Unclear – no mention of concealment throughout the paper.	High risk – no mention of blinding of participants throughout the paper. Patients and clinicians were most likely aware of the treatment, especially patients in the group with at-home bleaching had to be compliant and to know what to do. Patients in control group never received any treatment.	High risk (for esthetic improvement)– no mention of blinding throughout the paper. Unclear (for patient-reported outcomes) – In terms of sensitivity, satisfaction, and enamel surface, reported by the patients, no blinding is mentioned. Outcome is patient-reported and blinding of patients has been assessed in the previous domain.	Low risk – no drop-outs or patient losses are reported.	High risk – no protocol exist for the trial. Main outcome reported in detail. Results of the patient questionnaire are not fully reported, but only shortly discussed.	Unclear – residual bias cannot be excluded.
Loguercio 2007	Low risk – randomization took place by tossing a coin. "For each subject, two compound systems were randomly selected and designated "left" or "right". "A coin was tossed to determine whether Opalustre or PREMA would be used on the left or right side."	Unclear – unclear if allocation concealment was ensured. "All participants were informed of the nature and objectives of this study; however, they were unaware of the location of each material." "Two uniformed examiners, uniformed as to which product was used on which subjects, attempted to evaluate the clinical performance…"	Unclear – no mention of blinding throughout the paper. Blinding of patients is highly probable ("however, they were unaware of the location of each material"), whereas operator most likely knew which bleaching agent they were applying, as blinding is not easily applicable.	Low risk – outcome assessors were blinded. "Two blinded evaluators appraised both sides of the mouth using a visual scale system." Besides, operators applying the bleaching agents and examiners, were different people. Tooth sensitivity and surface was assessed by the patients themselves. Risk of detection bias highly improbable, as patients were most likely blinded and allocation concealed.	Unclear – not clearly reported. Even though all patients attended all treatments, nothing is mentioned about the follow-up. "All subjects had three clinical treatments." "The clinical aspect resulted from the microabrasion technique, which was evaluated at least 48 hours after completion of the clinical appointment…"	Unclear – no protocol exist for the trial. However, all in the trial mentioned pre-specified outcomes, such as esthetic improvement, patient satisfaction, and tooth surface, are reported in detail.	Unclear – residual bias cannot be excluded.
Loyola-Rodriguez 2003	Unclear – randomization description inadequate. "…patients were randomized into three groups of treatment, sample size was 38 subjects per group."	Unclear – nothing precisely mentioned. Highly probable that participants did not know assignment, as they did not know any treatment resp. group. "Both subjects and dentist were unaware of which treatment was involved."	Low risk – patients and clinicians are blinded. "A double blind clinical trial was done…" "Both subjects and dentist were unaware of which treatment was involved.	High risk – no blinding of evaluators is mentioned, but they were calibrated in advance.	Unclear – not clearly reported.	Low risk – no protocol exist for the trial. However, all in the trial mentioned pre-specified outcomes, such as esthetic improvement, tooth/gingival sensitivity, are reported in detail.	Unclear – residual bias cannot be excluded.

Appendix S4. Results of all included trials.

Nr	Trial	Ref	Exp	Outcome	Timing	Clus	MD (95% CI)	P	RR (95% CI)	P	Clinical relevance†
1	Bharath 2014	MAbr	Bleach	Apperance improvement$	post tx	yes	2.85 (2.36,3.35)	<0.001			Yes
2	Bharath 2014	MAbr	Bleach	Apperance improvement$	6 mos	yes	2.94 (2.48,3.40)	<0.001			Yes
3	Bharath 2014	MAbr	Bleach	Tooth sensitivity	post tx	yes	0.10 (-0.17,0.37)	0.46			-
4	Bharath 2014	MAbr	Bleach	Tooth sensitivity	1 mo	yes	No sensitivity				-
5	Bharath 2014	MAbr	Bleach	Tooth sensitivity	3 mos	yes	No sensitivity				-
6	Bharath 2014	MAbr	Bleach	Tooth sensitivity	6 mos	yes	No sensitivity				-
7	Castro 2014	MAbr	Mabr/Bleach	Lesion area	1 mo	No	-0.60 (-4.30,3.10)	0.75			-
8	Castro 2014	MAbr	Mabr/Bleach	Lesion area reduction	1 mo-BL	No	0.00 (-3.03,3.03)	1.00			-
9	Castro 2014	MAbr	Mabr/Bleach	Apperance improvement (patients)	aft	No	1.00 (-1.24,3.24)	0.38			-
10	Castro 2014	MAbr	Mabr/Bleach	Apperance improvement (dentists)	aft	No	0.00 (-2.83,2.83)	1.00			-
11	Gugnani 2017	Bleach (HP35%)	Resin infiltration (2')	Estethics improvement		No	3.60 (3.00,4.20)	<0.001			Yes
12	Gugnani 2017	Bleach (HP35%)	Resin infiltration (3')	Estethics improvement		No	3.63 (2.67,4.59)	<0.001			Yes
13	Gugnani 2017	Bleach (HP35%)	Bleach (HP35%) + resin infiltration (3')	Estethics improvement		No	3.45 (2.78,4.12)	<0.001			Yes
14	Gugnani 2017	Bleach (HP35%)	Resin infiltration (2')	Stain/opacities improvement		No	3.45 (2.81,4.09)	<0.001			Yes
15	Gugnani 2017	Bleach (HP35%)	Resin infiltration (3')	Stain/opacities improvement		No	3.65 (2.92,4.39)	<0.001			Yes
16	Gugnani 2017	Bleach (HP35%)	Bleach (HP35%) + resin infiltration (3')	Stain/opacities improvement		No	2.87 (2.03,3.71)	<0.001			Yes
17	Knosel 2008	Ctr	Bleach	Fluorosed-to-healthy enamel DE>3	BL				1.07 (0.82,1.39)	0.62	-
18	Knosel 2008	Ctr	Bleach	Fluorosed-to-healthy enamel DE>3	1 mo				0.68 (0.47,0.98)	0.04	No
19	Knosel 2008	Ctr	Bleach	Fluorosed-to-healthy enamel DE>3.7	BL				1.25 (0.89,1.75)	0.20	-
20	Knosel 2008	Ctr	Bleach	Fluorosed-to-healthy enamel DE>3.7	1 mo				0.68 (0.43,1.08)	0.10	-
21	Knosel 2008	Ctr	Bleach	L of fluorosed enamel change	1 mo-BL		4.24 (2.26,6.22)	<0.001			Yes
22	Knosel 2008	Ctr	Bleach	a of fluorosed enamel change	1 mo-BL		-0.99 (-1.42,-0.56)	<0.001			Yes
23	Knosel 2008	Ctr	Bleach	b of fluorosed enamel change	1 mo-BL		-5.20 (-7.55,-2.86)	<0.001			Yes

24	Knosel 2008	Ctr	Bleach	L of healthy enamel change	1 mo-BL		5.10 (2.83,7.37)	<0.001			Yes
25	Knosel 2008	Ctr	Bleach	a of healthy enamel change	1 mo-BL		-0.26 (-0.79,0.27)	0.33			-
26	Knosel 2008	Ctr	Bleach	b of healthy enamel change	1 mo-BL		-6.10 (-8.23,-3.97)	<0.001			Yes
27	Loguercio 2007	MAbr (PREMA)	MAbr (Opalustre)	Apperance improvement (dentists)	1 wk after app1	Yes	1.00 (0.72,1.28)	<0.001			Yes
28	Loguercio 2007	MAbr (PREMA)	MAbr (Opalustre)	Apperance improvement (dentists)	1 wk after app2	Yes	0.40 (0.10,0.70)	0.009			No
29	Loguercio 2007	MAbr (PREMA)	MAbr (Opalustre)	Apperance improvement (dentists)	1 wk after app3	Yes	0.20 (-0.24,0.64)	0.38			-
30	Loyola-Rodri-guez 2003	Bleach (CP10%)	Bleach (CP20%)	Sum TSIF>20	bef-aft				1.50 (0.27,8.48)	0.65	Yes
31	Loyola-Rodri-guez 2003	Bleach (CP10%)	Bleach (HP7.5%)	Sum TSIF>20	bef-aft				15.50 (3.99,60.23)	<0.001	Yes

† judged for statistically significant results as MD larger than half a standard deviation of the control response or RR larger than 30%

* medians converted to means for the analysis

$ all raters pooled together for the analysis

Ref, referent intervention; Exp, experimental group; Clus, clustered data; MD, mean difference; CI, confidence interval; RR, relative risk; MAbr, microabrasion; HP, hydrogen peroxide; Ctr, control (untreated); CP, carbamide peroxide.

Appendix S5. Further details to the review and deviations from protocol.

Author contributions

SNP conceived the idea and TDG wrote the first draft of the protocol. TDG, SNP, and TE revised the protocol. SNP performed the literature searches, while TDG extracted search hits, and did screening by title, abstract, fulltext, data extraction, and risk of bias assessment, while SNP checked all procedures afterwards in duplicate, and TE resolved discrepancies. SNP handled communications with trialists, performed the statistical analysis, and graded the quality of evidence with GRADE, while TDG checked this. TDG wrote the first draft of the manuscript. SNP and TE assisted in the interpretation of the results and revised the manuscript draft. SNP submitted the manuscript, is the guarantor and responsible for the accuracy of the data and for future updates of the review.

Deviations from protocol

- Additional analyses including subgroup analyses, meta-regressions, sensitivity analyses, and analyses of reporting bias were originally planned in the protocol, but could not be performed due to the limited number of available studies.
- The possibility of using network meta-analysis to directly compare all available interventions was considered during the protocol stage. This was however not possible due to the small number of interventions being compared in the identified trials and the sparse connections in the network.
- The Number Needed to Treat was planned to be used to clinically translate statistically significant RRs, but no such instance was encountered.

Acknowledgements

None.

Conflict of Interest

The authors of this manuscript certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.